

DESCRIPTION

OPTICALLY ACTIVE QUATERNARY AMMONIUM SALT, PRODUCTION METHOD
THEREOF, AND METHOD FOR PRODUCING OPTICALLY ACTIVE α -AMINO
5 ACID DERIVATIVE USING THE QUATERNARY AMMONIUM SALT

TECHNICAL FIELD

[0001]

The present invention relates to a novel axially chiral,
10 optically active spiro-quaternary ammonium salt and a
production method thereof, as well as to an intermediate for
use in the production of such an ammonium salt and a
production method thereof. The present invention further
relates to a method for stereoselectively producing an
15 optically active α -amino acid derivative, a useful
intermediate for the synthesis of pharmaceutical or
agrochemical products, by using the ammonium salt as a phase
transfer catalyst.

[0002]

20 The present invention also relates to a fluorine-
containing optically active quaternary ammonium salt and a
production method thereof, as well as to an intermediate
useful in the production of such a salt and a production
method thereof. The present invention still further relates to
25 a method for stereoselectively producing an optically active

α -amino acid derivative, a useful intermediate for the synthesis of pharmaceutical or agrochemical products, by using the fluorine-containing ammonium salt as a phase transfer catalyst, as well as to a method for recovering such a salt.

5 More specifically, the present invention relates to a method for recovering a fluorine-containing optically active quaternary ammonium salt by using an organic solvent with all hydrogen atoms substituted with fluorine atoms (i.e., fluorous solvent).

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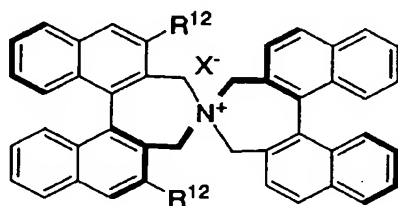
BACKGROUND ART

[0003]

As far as the background of the present invention is concerned, optically active spiro-quaternary ammonium salts

15 (A) through (N), which are collectively represented by the following formula (15), are known:

[0004]



(15)

[0005]

20 where

R¹² = a hydrogen atom and X⁻ = a bromide ion (Compound (A));

R¹² = a phenyl group and X⁻ = a bromide ion (Compound (B));

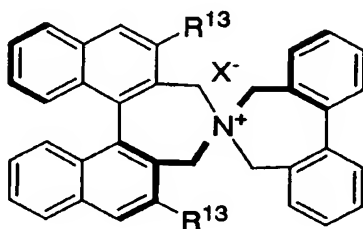
R^{12} = a β -naphthyl group and X^- = a bromide ion (Compound (C));
 R^{12} = a 3,4,5-trifluorophenyl group and X^- = a bromide ion
 (Compound (D));
 R^{12} = a 3,5-bistrifluoromethylphenyl group and X^- = a bromide
 5 ion (Compound (E));
 R^{12} = a 3,5-bis(3,5-bistrifluoromethylphenyl)phenyl group and
 X^- = a bromide ion (Compound (F));
 R^{12} = a 3,5-bis-*tert*-butylphenyl and X^- = a bromide ion
 (Compound (G));
 10 R^{12} = a 3,5-bis(3,5-bis-*tert*-butylphenyl)phenyl group and X^- =
 a bromide ion (Compound (H));
 R^{12} = a β -naphthyl group and X^- = a thiocyanic acid ion
 (Compound (I));
 R^{12} = a β -naphthyl group and X^- = a hydrogen sulfate ion
 15 (Compound (J));
 R^{12} = a 3,5-bistrifluoromethylphenyl group and X^- = a
 thiocyanic acid ion (Compound (K));
 R^{12} = a 3,5-bistrifluoromethylphenyl group and X^- = a hydrogen
 sulfate ion (Compound (L));
 20 R^{12} = a 3,4,5-trifluorophenyl group and X^- = a thiocyanic acid
 ion (Compound (M)); and
 R^{12} = a 3,4,5-trifluorophenyl group and X^- = a hydrogen sulfate
 ion (Compound (N)) (See, for example, Patent Article No. 1 for
 Compounds (A) through (D), Non-Patent Article No. 1 for
 25 Compounds (E) and (F), Non-Patent Article No. 2 for Compounds

(G) and (H), and Patent Article No. 2 for Compounds (I) through (N)).

[0006]

Also, optically active spiro-quaternary ammonium salts (O) and (P), which are collectively represented by the following formula (16), are known:

[0007]



(1 6)

[0008]

10 where

R¹³ = a hydrogen atom and X⁻ = a bromide ion (Compound (O));

and

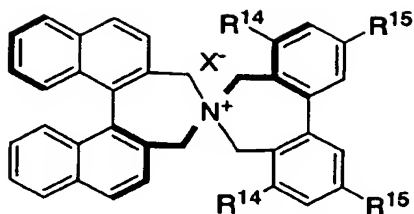
R¹³ = a β-naphthyl group and X⁻ = a bromide ion (Compound (P))

(See Patent Article No. 3).

15 [0009]

Furthermore, optically active spiro-quaternary ammonium salts (Q), (R), and (S), which are collectively represented by the following formula (17), are known:

[0010]



(1 7)

[0011]

where

R^{14} = a β -naphthyl group, R^{15} = a hydrogen atom, and X^- = a

5 bromide ion (Compound(Q);

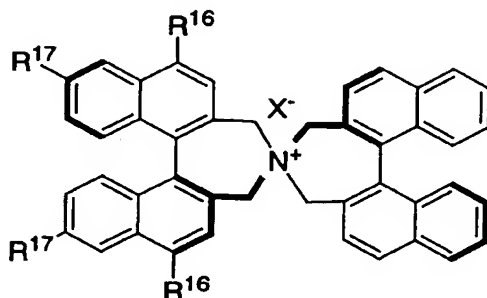
R^{14} = a 3,5-diphenylphenyl, R^{15} = a hydrogen atom, and X^- = a
bromide ion (Compound (R)); and

R^{14} = a 3,5-diphenylphenyl group, R^{15} = a phenyl group, and X^- =
a bromide ion (Compound (S)) (See Patent Article No. 3).

10 [0012]

Still further, optically active spiro-quaternary ammonium
salts (T), (U), and (V), which are collectively represented by
the following formula (18), are known:

[0013]



(1 8)

15

[0014]

where

$R^{16} = R^{17} =$ a phenyl group and $X^- =$ a bromide ion (Compound (T));

$R^{16} =$ a phenyl group, $R^{17} =$ a hydrogen atom, and $X^- =$ a bromide ion (Compound (U)); and

5 $R^{16} = R^{17} =$ a 3,5-diphenylphenyl group and $X^- =$ a bromide ion (Compound (V)) (See Non-Patent Article No. 3).

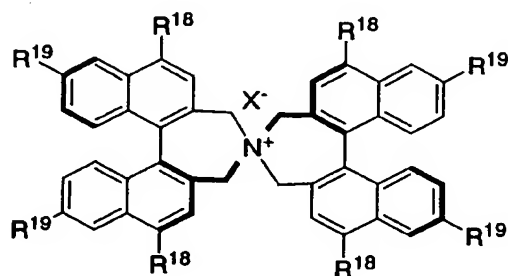
[0015]

Some of Compounds (A) through (V), for example Compound (D), are highly reactive and stereoselective. Nonetheless, the
10 asymmetric structure of these compounds results in as many as 13 to 16 different steps involved in the synthesis of the catalysts when commercially available optically active 1,1-bi-2-naphthol is used as the starting material.

[0016]

15 Still further, optically active spiro-quaternary ammonium salts (W), (X), (Y), and (Z), which are collectively represented by the following formula (19), are known:

[0017]



(19)

20 [0018]

where

$R^{18} = R^{19} =$ a phenyl group and X^- = a bromide ion (Compound (W));

R^{18} = a phenyl group, R^{19} = a hydrogen atom, and X^- = a bromide ion (Compound (X));

5 $R^{18} = R^{19} =$ a 3,5-diphenylphenyl group and X^- = a bromide ion (Compound (Y)); and

R^{18} = a 3,5-diphenylphenyl group, R^{19} = a hydrogen atom, and X^- = a bromide ion (Compound (Z)) (See, for example, Non-Patent Article No. 4). Since the two binaphthyl structures in these
10 compounds are identical to each other, the number of the steps involved in the synthesis of these catalysts is decreased to 8 to 11 steps.

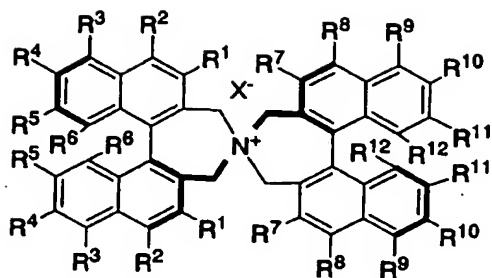
[0019]

In terms of catalytic performance, these catalysts show
15 high reactivity and high selectivity of 90% or above toward certain substrates when used in the asymmetric alkylation of glycine derivatives as described in the non-patent article. However, the catalysts have been proved to show decreased reactivity and selectivity toward some substrates such as
20 ethyl iodide.

[0020]

Of all the compounds represented by the following formula
(1):

[0021]



(1)

[0022]

only those in which the substituents on the aromatic rings are either hydrogen or carbon atoms are known. In addition, no compounds are known that are represented by the formula (1) with silicon atoms or silicon-containing compounds directly bound to the aromatic rings.

[0023]

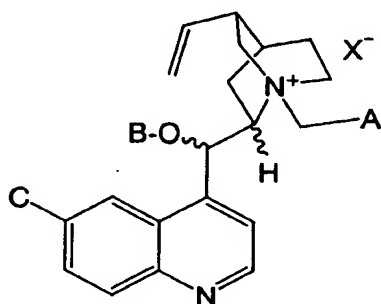
When optically active quaternary ammonium salts are used as phase-transfer catalysts in the production of optically active α -amino acid derivatives, the catalysts may be recovered afterwards for recycle. In one technique, this is done by neutralizing the aqueous phase with an acid after separation, extracting the aqueous phase with an organic solvent, and then purifying the extract by silica gel column chromatography (Non-Patent Article No. 5). While this technique is advantageous in that the activity of the recycled catalysts is retained, the recovery of the catalyst is only 72% and the technique involves many steps. For this reason, improvement in the recovery of the catalyst is required. Also, the process for recovering catalysts must be simplified enough

to be used in industrial applications.

[0024]

A much simpler approach to recover catalysts involves the use of a compound represented by the following formula (20):

5 [0025]



(20)

[0026]

This compound comprises an ammonium salt derivative of an optically active alkaloid (e.g., quinine, quinidine, cinchonine, and cinchonidine) bound to a polymer such as polystyrene and polyethylene glycol and is suitable for use as a chiral phase-transfer catalyst in the production of optically active α -amino acid derivatives (See Non-Patent Articles 6-8 for examples in which the polymer is introduced at the position 'A', Non-Patent Article 7 for an example in which the polymer is introduced at the position 'B', and Non-Patent Article No. 9 for an example in which the polymer is introduced at the position 'C'.).

[0027]

However, introduction of the polymer moiety may result in a significant decrease in the selectivity of the catalyst (See,

for example, Non-Patent Article No. 9). Even many of the catalysts that retain high stereoselectivity of 90% ee or above have not been shown to retain the catalytic performance when recycled following recovery (See, for example, Non-Patent Articles 7 and 8). Although no data is presented, only one example of practically recyclable catalysts is reported. In this case, a significant reduction of the selectivity is also experienced in this example when a different substrate is used (See, for example, Non-Patent Article No. 6).

[0028]

As optically active quaternary ammonium salts in which the backbone structure contains a fluorine atom as a C-F bond, alkaloid derivatives incorporating a fluorine-substituted benzyl group are known (See, for example, Non-Patent Articles 10 and 11). Also, optically active ammonium catalysts having such substituents as a 4-fluorophenyl group and a 3,4,5-trifluorophenyl group (See, for example, Non-Patent Article No. 12), a 3,5-bis(trifluoromethyl)phenyl group or a 3,5-bis(3,5-bis(trifluoromethyl)phenyl)phenyl group (See, for example, Non-Patent Article No. 13) are known as optically active quaternary ammonium salt derivatives having a chiral axis originating from binaphthyl.

[0029]

However, each of these compounds contains fluorine atoms in the form of 1 to 3 fluorine substituents on the benzene

ring or in the form of 1 to 8 trifluoromethyl groups: No
optically active quaternary ammonium salts have been known to
date that contain fluorine atoms in the form of perfluoro
groups, or substituents consisting of two or more carbon atoms
5 with all the hydrogen atoms substituted with fluorine atoms.

[0030]

Different perfluoro alkyl-containing optically active
asymmetric catalyst ligands are known, including axially
chiral binaphthol derivatives (See, for example, Non-Patent
10 Articles No. 14-18), optically active salen derivatives (See,
for example, Non-Patent Articles No. 19-22), optically active
ephedrine derivatives (See, for example, Non-Patent Article No.
23), and optically active aminothiulates (See, for example,
Non-Patent Article No. 24). Each of these compounds is used in
15 the synthesis of optically active compounds different from the
compounds of the present invention. Attempts for recovery and
recycle have been made for some of the compounds.

[0031]

However, except for the asymmetric protonation agents
20 used in stoichiometric amounts (Non-Patent Article 14), each
compound has to be catalytically prepared through the
formation of oxygen-metal bonds or complexes: No optically
active organic catalysts are known that themselves serve as an
asymmetric catalyst. In particular, no optically active
25 quaternary ammonium salts are known that contain perfluoro

alkyl groups consisting of two or more carbon atoms. Nor are any examples known of the use of the salts as asymmetric catalysts or as phase-transfer catalysts. No examples are known in which the phase transfer catalytic reaction is

5 carried out in a three-phase system consisting of organic, aqueous and fluorous phases, nor are any examples described of the use of fluorous solvents to separate/purify the salts or to recover only the catalyst from the catalyst-containing mixture remaining after the reaction. No examples are known of

10 recovering the salts to serve as catalysts in a substantially quantitative manner, nor are any examples known in which the salts are recovered in a separate phase of a fluorous solvent and the recovered salts are recycled as an asymmetric catalyst in the same reaction, and which demonstrate that the

15 performance of the catalyst as measured by the reactivity and stereoselectivity are retained.

[Patent Article No. 1] Japanese Patent Laid-Open
Publication No. 2001-48866

[Patent Article No. 2] Japanese Patent Laid-Open

20 Publication No. 2002-173492

[Patent Article No. 3] Japanese Patent Laid-Open
Publication No. 2002-326992

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DISCLOSURE OF THE INVENTION

PROBLEMS TO BE SOLVED BY THE INVENTION

[0032]

25 In view of the above-described state of the background

art, objects of the present invention are:

- 1) to provide a novel axially chiral, optically active spiro-quaternary ammonium salt, that when used as a phase-transfer catalyst in the asymmetric alkylation of a glycine derivative,
5 gives a high stereoselectivity of 90% ee or above and has a novel substituent to provide steric hindrance that allows the salt to be applied to a broader range of substrates with high selectivity, and in particular, to provide a compound in which each ring of the spiro-structure has the same structure and
10 which is thus advantageous in terms of the number of steps involved in the synthesis of the catalyst;
- 2) to provide a method for producing the salts;
- 3) to provide an intermediate for use in the production of the salts, and a method for producing the intermediate; and
15 4) to provide a method for using the ammonium salts as a phase transfer catalyst and thus stereoselectively producing an optically active α -amino acid derivative suitable for use as an intermediate in the synthesis of pharmaceutical or agrochemical products.

20 Further objects of the present invention are:

- 5) to provide a novel optically active quaternary ammonium salt, that when used as a phase-transfer catalyst in the asymmetric alkylation of a glycine derivative, gives a high stereoselectivity of 90% ee or above and is readily recovered
25 after the reaction;

6) to provide the salt that retains its catalytic performance when recycled;

7) to provide a method for readily recovering, separating, and purifying the salt at high yield after the reaction;

5 8) to provide a method for producing the salt;

9) to provide a method for using the salt as a phase-transfer catalyst and thus stereoselectively producing an optically active α -amino acid derivative suitable for use as an intermediate in the synthesis of pharmaceutical or

10 agrochemical products; and

10) to recover the salt used in the reaction and ensure that high catalytic performance is retained in the recycled salt.

MEANS FOR SOLVING THE PROBLEMS

[0033]

15 In an effort to address the objects 1) through 4) above, the present inventor has conducted an extensive study and found a novel axially chiral, optically active ammonium salt that incorporates a novel alkyl- or aryl-substituted silyl group as a substituent on the binaphthyl aromatic ring.

20 [0034]

In a further effort to address the objects 5) through 10) above, the present inventor has conducted extensive study and found a novel axially chiral, optically active ammonium salt that includes a perfluoro group with all hydrogen atoms
25 substituted with fluorine atoms, and such an ammonium salt,

after use as a chiral phase-transfer catalyst, can be extracted for recycle with a fluorous solvent that has all hydrogen atoms substituted with fluorine atoms. It is these findings that led to the present invention.

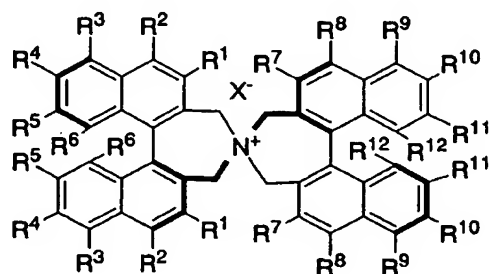
5 [0035]

Accordingly, the present invention concerns an optically active quaternary ammonium salt, a method for producing the ammonium salt, a method for producing an optically active α -amino acid derivative using the ammonium salt, and a method
10 for recovering the ammonium salt, as follows.

[0036]

[1] An optically active quaternary ammonium salt, represented by the following formula (1a):

[0037]



(1 a)

15

[0038]

[wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, and R¹² are each independently a hydrogen atom, a methyl group, an ethyl group, a straight, branched or cyclic alkyl group having 3 to
20 18 carbon atoms, a straight, branched or cyclic heteroalkyl group having 3 to 18 carbon atoms, a straight, branched or

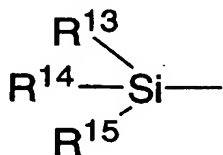
cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 35 carbon atoms, or a heteroaralkyl group having 5 to 35 carbon atoms;

[0039]

with the proviso that at least one of R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , R^{11} , and R^{12} is a substituent represented by the

10 following formula (2a):

[0040]



(2 a)

[0041]

(wherein R^{13} , R^{14} , and R^{15} are each independently a methyl group,

15 an ethyl group, a vinyl group, a straight, branched or cyclic

alkyl group having 3 to 18 carbon atoms, a straight, branched

or cyclic alkenyl group having 3 to 18 carbon atoms, a

straight, branched or cyclic alkynyl group having 3 to 18

carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an

20 aryl group having 5 to 20 carbon atoms, an aralkyl group

having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms.);

[0042]

X⁻ is a fluorine ion, a chloride ion, a bromide ion, an iodide ion, a p-toluenesulfonic acid ion, a hydroxide ion, a thiocyanate ion, a hydrogen sulfate ion, a perchloric acid ion, or a hexafluorophosphoric acid ion; and the two binaphthyl moieties each have a chiral axis so that the absolute configurations of the two binaphthyl moieties are (R, R) or (S, S)].

[0043]

[2] The optically active quaternary ammonium salt according to [1] above, wherein R¹ and R⁷, R³ and R⁹, R⁴ and R¹⁰, R⁵ and R¹¹, and R⁶ and R¹² in the formula (1a) are in each case identical to one another; R² and R⁸ are identical to one another and are each represented by the formula (2a); and X⁻ is a fluorine ion, a chloride ion, a bromide ion, an iodide ion, a p-toluenesulfonic acid ion, or a hydroxide ion.

[0044]

[3] The optically active quaternary ammonium salt according to [1] above, wherein R¹, R³, R⁵, R⁶, R⁷, R⁹, R¹¹, and R¹² in the formula (1a) are each independently a hydrogen atom; R², R⁴, R⁸, and R¹⁰ are identical to one another and are each represented by the formula (2a); and X⁻ is a chloride ion, a bromide ion, an iodide ion, or a p-toluenesulfonic acid ion.

[0045]

[4] The optically active quaternary ammonium salt according to [1] above, wherein in the formula (1a), R¹ and R⁷, R³ and R⁹, R⁴

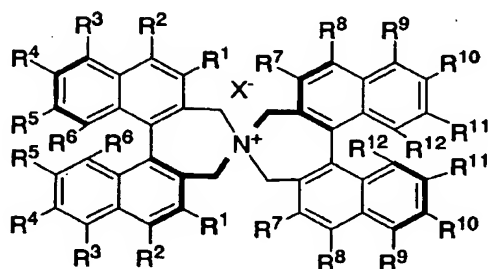
and R^{10} , R^5 and R^{11} , and R^6 and R^{12} are in each case identical to one another, R^2 and R^8 are identical to one another and are each represented by the formula (2a), and X^- is a bromide ion; and R^{13} , R^{14} and R^{15} in the formula (2a) are each independently

5 a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-octyl group, and a phenyl group.

[0046]

10 [5] An optically active quaternary ammonium salt represented by the following formula (1b):

[0047]



(1 b)

[0048]

15 [wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , R^{11} , and R^{12} are each independently a hydrogen atom, a halogen atom, a methyl group that may or may not be substituted with fluorine, an ethyl group that may or may not be substituted with fluorine, a straight, branched or cyclic alkyl group that has 3 to 18

20 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic heteroalkyl group that has 3 to

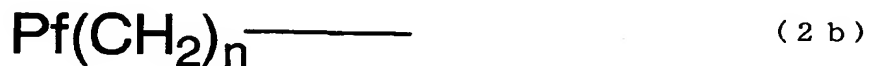
18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkynyl group

5 that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, an alkoxyl group that has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and may or may not be substituted with fluorine, an aralkyl group that has 5 to
10 35 carbon atoms and may or may not be substituted with fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine;

[0049]

with the proviso that at least one of R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 ,
15 R^8 , R^9 , R^{10} , R^{11} , and R^{12} is a substituent represented by the following formula (2b):

[0050]



[0051]

20 (wherein Pf is a straight, branched or cyclic alkyl group that has 2 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight,

branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, or a heteroaralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms. n is an integer from 0 to 4.), and/or by the following formula (2c):

10 [0052]



[0053]

(wherein Pf and n are as defined in the formula (2b) above,

[0054]

15 R¹³ and R¹⁴ are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon

atoms.);

[0055]

X⁻ is a fluoride ion, a chloride ion, a bromide ion, an iodide ion, a p-toluenesulfonic acid ion, a hydroxide ion, a

5 thiocyanate ion, a hydrogen sulfate ion, a perchloric acid ion, or a hexafluorophosphoric acid ion; and the two binaphthyl moieties each have a chiral axis so that the absolute configurations of the two binaphthyl moieties are (R, R) or (S, S)].

10 [0056]

[6] The optically active quaternary ammonium salt according to [5] above, wherein R¹ and R⁷, R³ and R⁹, R⁴ and R¹⁰, R⁵ and R¹¹, and R⁶ and R¹² in the formula (1b) are in each case identical to one another; R² and R⁸ are identical to one another and are
15 each represented by the formula (2a); and X⁻ is a fluorine ion, a chloride ion, a bromide ion, an iodide ion, a p-toluenesulfonic acid ion, a thiocyanate ion, a hydrogen sulfate ion, or a hydroxide ion.

[0057]

20 [7] The optically active quaternary ammonium salt according to [5] above, wherein R¹, R³, R⁵, R⁶, R⁷, R⁹, R¹¹, and R¹² in the formula (1b) are each independently a hydrogen atom; R², R⁴, R⁸, and R¹⁰ are identical to one another and are each represented by the formula (2c); and X⁻ is a chloride ion, a bromide ion,
25 an iodide ion, or a p-toluenesulfonic acid ion.

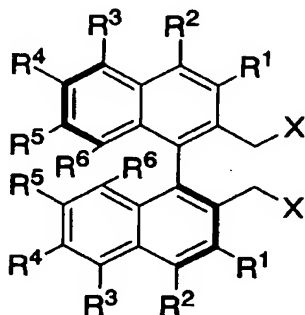
[0058]

[8] The optically active quaternary ammonium salt according to [5] above, wherein in the formula (1b), R^1 and R^7 , R^3 and R^9 , R^4 and R^{10} , R^5 and R^{11} , and R^6 and R^{12} are in each case identical to one another, and X^- is a bromide ion; and in the formula (2c), n is 2, R^{13} and R^{14} are each a methyl group, and Pf is an n -octyl group having all the hydrogen atoms substituted with fluorine atoms.

[0059]

[9] An optically active binaphthyl compound represented by the following formula (3a):

[0060]



(3 a)

[0061]

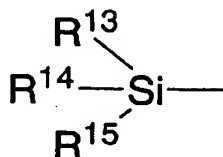
[wherein R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 are each independently a hydrogen atom, a methyl group, an ethyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic heteroalkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic

alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 35 carbon atoms, or a heteroaralkyl group having 5 to 35 carbon atoms;

5 [0062]

with the proviso that at least one of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 is a substituent represented by the following formula (2a):

[0063]



(2 a)

10 [0064]

(wherein R^{13} , R^{14} , and R^{15} are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a

15 straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms); X is a chlorine atom, a bromine atom, an
20 iodine atom, or a p-toluenesulfonyloxy group; and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

[0065]

[10] The optically active binaphthyl compound according to [9] above, wherein R^1 , R^3 , R^5 , and R^6 in the formula (3a) are each independently a hydrogen atom; and R^2 and R^4 are identical to
5 one another and are each represented by the formula (2a).

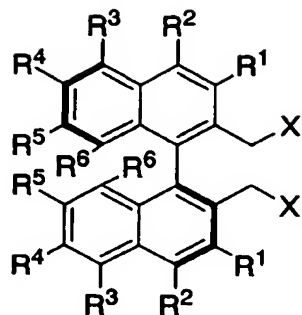
[0066]

[11] The optically active binaphthyl compound according to [9] above, wherein in the formula (3a), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, R^2 and R^4 are identical to one
10 another and are each represented by the formula (2a), and X is a bromine atom; and R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group,
15 a sec-butyl group, a tert-butyl group, an n-octyl group, and a phenyl group.

[0067]

[12] An optically active binaphthyl compound represented by the following formula (3b):

[0068]



(3 b)

[0069]

[wherein R¹, R², R³, R⁴, R⁵ and R⁶ are each independently a hydrogen atom, a halogen atom, a methyl group that may or may not be substituted with fluorine, an ethyl group that may or may not be substituted with fluorine, a straight, branched or cyclic alkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic heteroalkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, an alkoxyl group that has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and may or may not be substituted with fluorine, an aralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with

fluorine;

[0070]

with the proviso that at least one of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 is a substituent represented by the following formula (2b):

5 [0071]



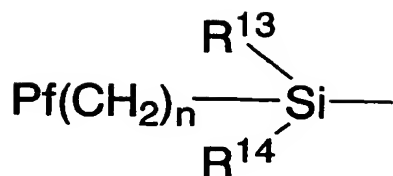
[0072]

(wherein Pf is a straight, branched or cyclic alkyl group that has 2 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, or a heteroaralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms,

[0073]

and n is an integer from 0 to 4.), and/or by the following formula (2c):

[0074]



(2 c)

[0075]

(wherein Pf and n are as defined in the formula (2b) above,

[0076]

- 5 R¹³ and R¹⁴ are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms,
10 an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms.);

[0077]

- 15 X is a chlorine atom, a bromine atom, an iodine atom, or a p-toluenesulfonyloxy group; and

[0078]

the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

- 20 [13] The optically active binaphthyl compound according to [12] above, wherein R¹, R³, R⁵, and R⁶ in the formula (3b) are each independently a hydrogen atom; and R² and R⁴ are identical

to one another and are each represented by the formula (2c).

[0079]

[14] The optically active binaphthyl compound according to

[12] above, wherein in the formula (3b), R^1 , R^3 , R^5 , and R^6 are

5 each independently a hydrogen atom, R^2 and R^4 are identical to one another and are each represented by the formula (2c), and X is a bromine atom; and in the formula (2c), n is 2, R^{13} and R^{14} are each a methyl group, and Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms.

10 [0080]

[15] A method for producing the optically active quaternary ammonium salt according to any of [1] to [8] above represented by the formula (1a) or (1b) in which X^- is a chloride ion, a bromide ion, an iodide ion, or a p-toluenesulfonic acid ion,

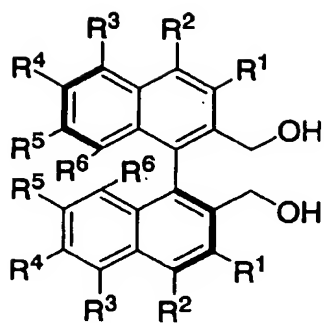
15 characterized in that the optically active binaphthyl compound according to any of claim 9 to claim 14 above represented by the formula (3a) or (3b) is reacted with ammonia.

[0081]

[16] An optically active binaphthyl dihydroxyl compound

20 represented by the following formula (4a):

[0082]



(4 a)

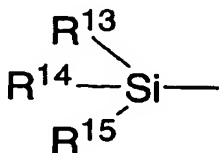
[0083]

[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a methyl group, an ethyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic heteroalkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 35 carbon atoms, or a heteroaralkyl group having 5 to 35 carbon atoms;

[0084]

with the proviso that at least one of R¹, R², R³, R⁴, R⁵, and R⁶ is a substituent represented by the following formula (2a):

[0085]



(2 a)

[0086]

(wherein R¹³, R¹⁴, and R¹⁵ are each independently a methyl group,

an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms); and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

[0087]

[17] The optically active binaphthyl dihydroxyl compound according to [16] above, wherein R^1 , R^3 , R^5 , and R^6 in the formula (4a) are each independently a hydrogen atom; and R^2 and R^4 are identical to one another and are each represented by the formula (2a).

[0088]

[18] The optically active binaphthyl dihydroxyl compound according to [16] above, wherein in the formula (4a), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2a); and R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-

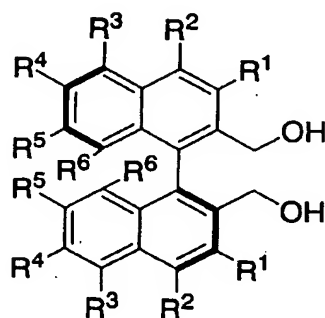
butyl group, a *tert*-butyl group, an n-octyl group, and a phenyl group.

[0089]

[19] An optically active binaphthyl dihydroxyl compound

5 represented by the following formula (4b):

[0090]



(4 b)

[0091]

[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a
10 hydrogen atom, a halogen atom, a methyl group that may or may
not be substituted with fluorine, an ethyl group that may or
may not be substituted with fluorine, a straight, branched or
cyclic alkyl group that has 3 to 18 carbon atoms and may or
may not be substituted with fluorine, a straight, branched or
15 cyclic heteroalkyl group that has 3 to 18 carbon atoms and may
or may not be substituted with fluorine, a straight, branched
or cyclic alkenyl group that has 3 to 18 carbon atoms and may
or may not be substituted with fluorine, a straight, branched
or cyclic alkynyl group that has 3 to 18 carbon atoms and may
20 or may not be substituted with fluorine, an alkoxyl group that

has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and may or may not be substituted with fluorine, an aralkyl group that has 5 to 35 carbon atoms and may or may not be

5 substituted with fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine;

[0092]

with the proviso that at least one of R¹, R², R³, R⁴, R⁵, and R⁶ is a substituent represented by the following formula (2b):

[0093]

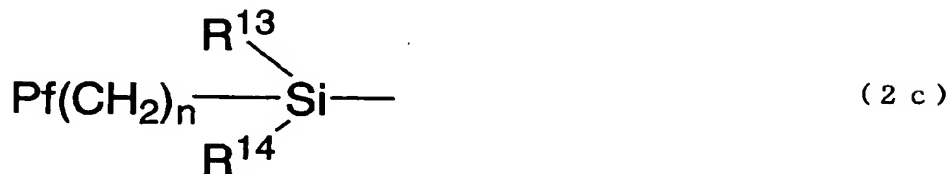


[0094]

(wherein Pf is a straight, branched or cyclic alkyl group that
15 has 2 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms
20 and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, or a heteroaralkyl

group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, and n is an integer from 0 to 4.), and/or by the following formula (2c):

[0095]



5

[0096]

(wherein Pf and n are as defined in the formula (2b) above,

[0097]

R^{13} and R^{14} are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms.); and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

20 [0098]

[20] The optically active binaphthyl dihydroxyl compound according to [19] above, wherein R^1 , R^3 , R^5 , and R^6 in the

formula (4b) are each independently a hydrogen atom; and R^2 and R^4 are identical to one another and are each represented by the formula (2c).

[0099]

- 5 [21] The optically active binaphthyl dihydroxyl compound according to [19] claim 10 above, wherein in the formula (4b), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2c); and in the formula (2c), n is 2, R^{13} and
- 10 R^{14} are each a methyl group, and Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms.

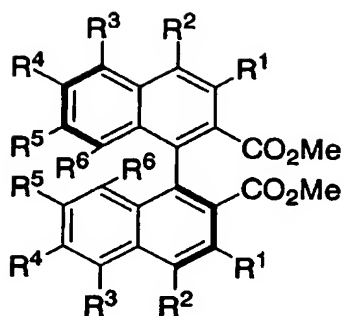
[0100]

- [22] A method for producing the optically active binaphthyl compound of the formula (3a) or (3b) according to any of [9] to [14], characterized in that the optically active binaphthyl dihydroxyl compound of the formula (4a) or (4b) according to
- 15 any of [16] to [21] is reacted with a halogen source or p-toluenesulfonyl chloride.

[0101]

- 20 [23] An optically active binaphthyl diester compound represented by the following formula (5a):

[0102]



(5 a)

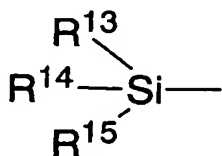
[0103]

[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a methyl group, an ethyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic heteroalkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 35 carbon atoms, or a heteroaralkyl group having 5 to 35 carbon atoms;

[0104]

with the proviso that at least one of R¹, R², R³, R⁴, R⁵, and R⁶ is a substituent represented by the following formula (2a):

[0105]



(2 a)

[0106]

(wherein R^{13} , R^{14} , and R^{15} are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a

5 straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms); and the binaphthyl moiety has a chiral
10 axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

[0107]

[24] The optically active binaphthyl diester compound according to [23] above, wherein R^1 , R^3 , R^5 , and R^6 in the
15 formula (3a) are each independently a hydrogen atom; and R^2 and R^4 are identical to one another and are each represented by the formula (2a).

[0108]

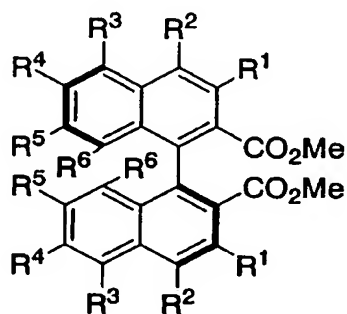
[25] The optically active binaphthyl diester compound
20 according to [23] above, wherein in the formula (5a), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, R^2 and R^4 are identical to one another and are each represented by the formula (2a), and R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting
25 of a methyl group, an ethyl group, an n-propyl group, an

isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-octyl group, and a phenyl group.

[0109]

- 5 [26] An optically active binaphthyl diester compound represented by the following formula (5b):

[0110]



(5 b)

[0111]

- 10 [wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a halogen atom, a methyl group that may or may not be substituted with fluorine, an ethyl group that may or may not be substituted with fluorine, a straight, branched or cyclic alkyl group that has 3 to 18 carbon atoms and may or
15 may not be substituted with fluorine, a straight, branched or cyclic heteroalkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and may
20

or may not be substituted with fluorine, an alkoxyl group that has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and may or may not be substituted with fluorine, an aralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine;

[0112]

with the proviso that at least one of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 is a substituent represented by the following formula (2b):

[0113]

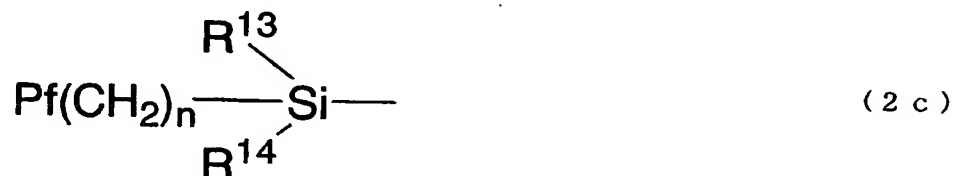


[0114]

(wherein Pf is a straight, branched or cyclic alkyl group that has 2 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen

atoms substituted with fluorine atoms, or a heteroaralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, and n is an integer from 0 to 4.), and/or by the following formula (2c):

5 [0115]



[0116]

(wherein Pf and n are as defined in the formula (2b) above,

[0117]

10 R¹³ and R¹⁴ are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms,
15 an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms.); and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or
20 (S)].

[0118]

[27] The optically active binaphthyl diester compound according to [26] above, wherein R¹, R³, R⁵, and R⁶ in the

formula (5b) are each independently a hydrogen atom; and R^2 and R^4 are identical to one another and are each represented by the formula (2c).

[0119]

- 5 [28] The optically active binaphthyl diester compound according to [26] above, wherein in the formula (5b), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2c); and in the formula (2c), n is 2, R^{13} and R^{14} are
10 each a methyl group, and Pf is an n -octyl group having all the hydrogen atoms substituted with fluorine atoms.

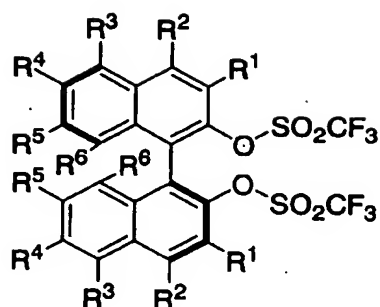
[0120]

- [29] A method for producing the compound according to any of [16] to [21] above represented by the formula (4a) or (4b),
15 characterized in that the optically active binaphthyl diester compound according to any of [23] to [28] above represented by the formula (5a) or (5b) is reacted with a hydrogen anion.

[0121]

- [30] An optically active binaphthyl compound represented by
20 the following formula (6a):

[0122]



(6 a)

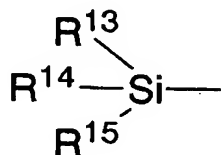
[0123]

[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a methyl group, an ethyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic heteroalkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 35 carbon atoms, or a heteroaralkyl group having 5 to 35 carbon atoms;

[0124]

with the proviso that at least one of R¹, R², R³, R⁴, R⁵, and R⁶ is a substituent represented by the following formula (2a):

[0125]



(2 a)

[0126]

(wherein R¹³, R¹⁴, and R¹⁵ are each independently a methyl group,

an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms); and

[0127]

10 the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

[31] The optically active binaphthyl compound according to [30] above, wherein R^1 , R^3 , R^5 , and R^6 in the formula (6a) are each independently a hydrogen atom; and R^2 and R^4 are identical to one another and are each represented by the formula (2a).

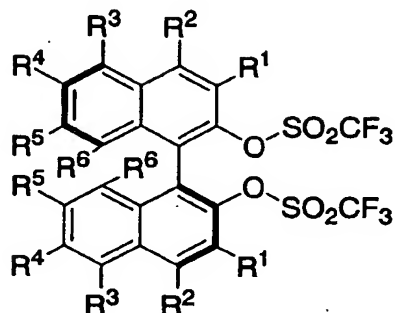
15 [0128]

[32] The optically active binaphthyl compound according to [30] above, wherein in the formula (6a), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2a); and R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-octyl group, and a phenyl group.

[0129]

[33] An optically active binaphthyl compound represented by the following formula (6b):

[0130]



(6 b)

5

[0131]

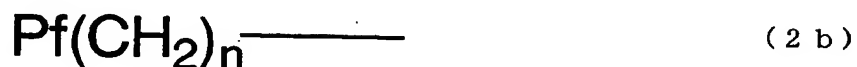
[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a halogen atom, a methyl group that may or may not be substituted with fluorine, an ethyl group that may or may not be substituted with fluorine, a straight, branched or cyclic alkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic heteroalkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, an alkoxy group that has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and

may or may not be substituted with fluorine, an aralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine;

[0132]

with the proviso that at least one of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 is a substituent represented by the following formula (2b):

[0133]



[0134]

(wherein Pf is a straight, branched or cyclic alkyl group that has 2 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, or a heteroaralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, and n is an integer

from 0 to 4.), and/or by the following formula (2c):

[0135]



[0136]

5 (wherein Pf and n are as defined in the formula (2b) above,

[0137]

R¹³ and R¹⁴ are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms.); and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

[0138]

[34] The optically active binaphthyl compound according to [33] above, wherein R¹, R³, R⁵, and R⁶ in the formula (6b) are each independently a hydrogen atom; and R² and R⁴ are identical to one another and are each represented by the formula (2c).

[0139]

[35] The optically active binaphthyl compound according to [33] above, wherein in the formula (6b), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2c);
 5 and in the formula (2c), n is 2, R^{13} and R^{14} are each a methyl group, and Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms.

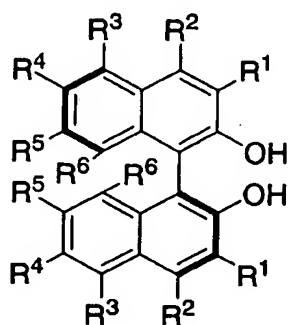
[0140]

[36] A method for producing the optically active binaphthyl diester compound of the formula (5a) or (5b) according to any
 10 of [23] to [28], characterized in that the optically active binaphthyl compound of the formula (6a) or (6b) according to any of [30] to [35] is reacted with carbon monoxide and methanol in the presence of a palladium catalyst and an
 15 organic base.

[0141]

[37] An optically active binaphthol compound represented by the following formula (7a):

[0142]



(7 a)

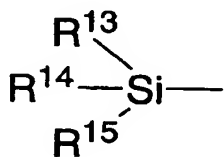
[0143]

[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a methyl group, an ethyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic heteroalkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 35 carbon atoms, or a heteroaralkyl group having 5 to 35 carbon atoms;

[0144]

with the proviso that at least one of R¹, R², R³, R⁴, R⁵, and R⁶ is a substituent represented by the following formula (2a):

[0145]



(2 a)

[0146]

(wherein R¹³, R¹⁴, and R¹⁵ are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an

aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms); and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

[0147]

[38] The optically active binaphthol compound according to [37] above, wherein R^1 , R^3 , R^5 , and R^6 in the formula (7a) are each independently a hydrogen atom; and R^2 and R^4 are identical to one another and are each represented by the formula (2a).

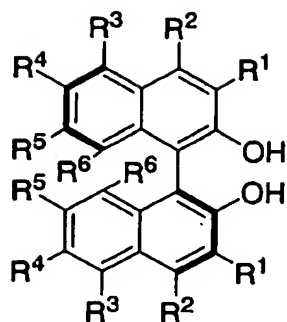
[0148]

[39] The optically active binaphthol compound according to [37] above, wherein in the formula (7a), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, R^2 and R^4 are identical to one another and are each represented by the formula (2a), and R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-octyl group, and a phenyl group.

[0149]

[40] An optically active binaphthol compound represented by the following formula (7b):

[0150]



(7 b)

[0151]

[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a halogen atom, a methyl group that may or may not be substituted with fluorine, an ethyl group that may or may not be substituted with fluorine, a straight, branched or cyclic alkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic heteroalkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, an alkoxy group that has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and may or may not be substituted with fluorine, an aralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with

fluorine;

[0152]

with the proviso that at least one of R¹, R², R³, R⁴, R⁵, and R⁶ is a substituent represented by the following formula (2b):

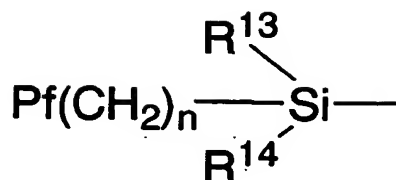
5 [0153]



[0154]

(wherein Pf is a straight, branched or cyclic alkyl group that has 2 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, or a heteroaralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, and n is an integer from 0 to 4.), and/or by the following formula (2c):

[0155]



(2 c)

[0156]

(wherein Pf and n are as defined in the formula (2b) above,

[0157]

- 5 R¹³ and R¹⁴ are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms,
10 an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms.); and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or
15 (S)].

[0158]

- [41] The optically active binaphthol compound according to
[40] above, wherein R¹, R³, R⁵, and R⁶ in the formula (7b) are each independently a hydrogen atom; and R² and R⁴ are identical
20 to one another and are each represented by the formula (2c).

[0159]

- [42] The optically active binaphthol compound according to

[40] above, wherein in the formula (7b), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2c); and in the formula (2c), n is 2, R^{13} and R^{14} are each a methyl group, and Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms.

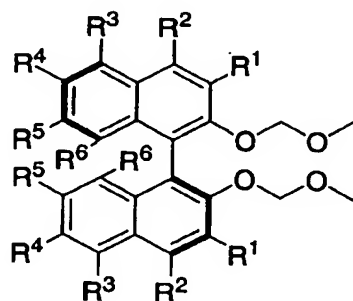
[0160]

[43] A method for producing the optically active binaphthyl compound according to any of [30] to [35] above represented by the formula (6a) or (6b), characterized in that the optically active binaphthol compound according to any of [37] to [42] above represented by the formula (7a) or (7b) is reacted with a triflating agent.

[0161]

[44] An optically active binaphthyl bis-methoxymethyl ether compound represented by the following formula (8a):

[0162]



(8 a)

[0163]

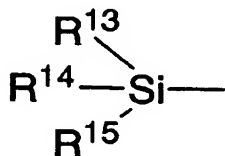
[wherein R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 are each independently a hydrogen atom, a methyl group, an ethyl group, a straight,

branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic heteroalkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 35 carbon atoms, or a heteroaralkyl group having 5 to 35 carbon atoms;

[0164]

with the proviso that at least one of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 is a substituent represented by the following formula (2a):

[0165]



(2 a)

[0166]

(wherein R^{13} , R^{14} , and R^{15} are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms); and the binaphthyl moiety has a chiral

axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

[0167]

[45] The optically active binaphthyl bis-methoxymethyl ether compound according to [44] above, wherein R^1 , R^3 , R^5 , and R^6 in the formula (8a) are each independently a hydrogen atom; and R^2 and R^4 are identical to one another and are each represented by the formula (2a).

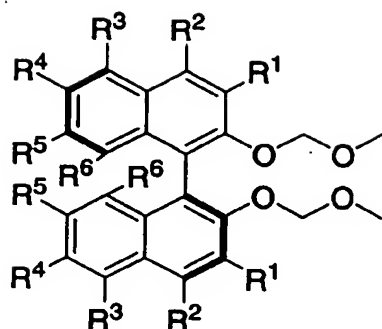
[0168]

[46] The optically active binaphthyl bis-methoxymethyl ether compound according to [44] above, wherein in the formula (8a), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, R^2 and R^4 are identical to one another and are each represented by the formula (2a), and R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-octyl group, and a phenyl group.

[0169]

[47] An optically active binaphthyl bis-methoxymethyl ether compound represented by the following formula (8b):

[0170]



(8 b)

[0171]

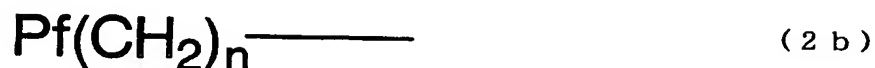
[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a halogen atom, a methyl group that may or may not be substituted with fluorine, an ethyl group that may or may not be substituted with fluorine, a straight, branched or cyclic alkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic heteroalkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, an alkoxyl group that has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and may or may not be substituted with fluorine, an aralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with

fluorine;

[0172]

with the proviso that at least one of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 is a substituent represented by the following formula (2b):

5 [0173]



[0174]

(wherein Pf is a straight, branched or cyclic alkyl group that has 2 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, or a heteroaralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, and n is an integer from 0 to 4.), and/or by the following formula (2c):

[0175]



[0176]

(wherein Pf and n are as defined in the formula (2b) above,

[0177]

- 5 R¹³ and R¹⁴ are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms.); and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or
10 (S)].

[0178]

- [48] The optically active binaphthyl bis-methoxymethyl ether compound according to [47] above, wherein R¹, R³, R⁵, and R⁶ in the formula (8b) are each independently a hydrogen atom; and R²
20 and R⁴ are identical to one another and are each represented by the formula (2c).

[0179]

[49] The optically active binaphthyl bis-methoxymethyl ether compound according to [47] above, wherein in the formula (8b), R^1 , R^3 , R^5 , and R^6 are each independently a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented
 5 by the formula (2c); and in the formula (2c), n is 2, R^{13} and R^{14} are each a methyl group, and Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms.

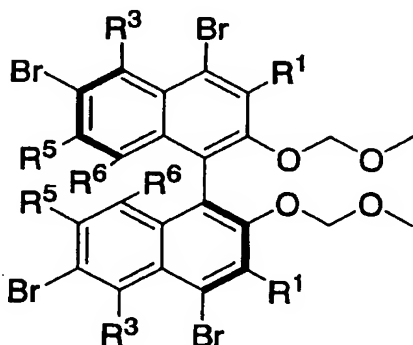
[0180]

[50] A method for producing the optically active binaphthol
 10 compound according to any of [37] to [42] above represented by the formula (7a) or (7b), characterized in that the optically active binaphthyl bis-methoxymethyl ether compound according to any of [44] to [49] above represented by the formula (8a) or (8b) is reacted with an acid.

[0181]

[51] An optically active binaphthyl bis-methoxymethyl ether compound represented by the following formula (9a):

[0182]



(9 a)

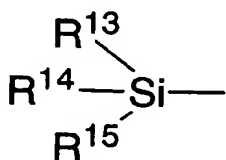
[0183]

[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a methyl group, an ethyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic heteroalkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 35 carbon atoms, or a heteroaralkyl group having 5 to 35 carbon atoms;

[0184]

with the proviso that at least one of R¹, R², R³, R⁴, R⁵, and R⁶ is a substituent represented by the following formula (2a):

[0185]



(2 a)

[0186]

(wherein R¹³, R¹⁴, and R¹⁵ are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group

having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms); and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

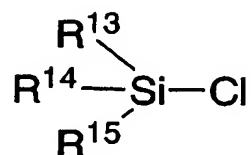
5 [0187]

[52] The optically active binaphthyl bis-methoxymethyl ether compound according to [51] above, wherein R^1 , R^3 , R^5 , and R^6 in the formula (9a) are each independently a hydrogen atom.

[0188]

10 [53] A method for producing the optically active binaphthyl bis-methoxymethyl ether compound according to any of [44] to [46] above represented by the formula (8a), comprising reacting with an alkyl lithium the optically active binaphthyl bis-methoxymethyl ether compound according to any of [51] or
15 [52] above represented by the formula (9a), and subsequently reacting with the reaction product a silyl chloride represented by the following formula (10a):

[0189]



(10a)

20 [0190]

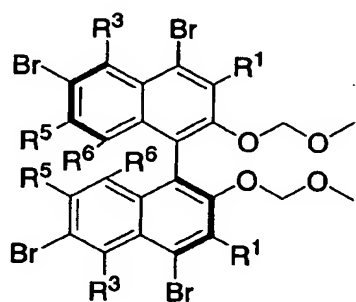
(wherein R^{13} , R^{14} , and R^{15} are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched

or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms).

[0191]

[54] A method for producing the optically active binaphthyl bis-methoxymethyl ether compound according to any of claims 47 to 49 represented by the formula (8b), comprising reacting with an alkyl lithium an optically active binaphthyl bis-methoxymethyl ether compound represented by the following formula (9b):

[0192]



(9 b)

[0193]

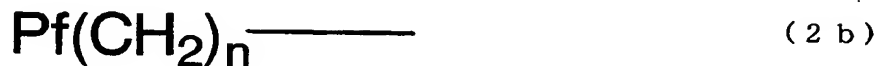
[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a halogen atom, a methyl group that may or may not be substituted with fluorine, an ethyl group that may or may not be substituted with fluorine, a straight, branched or

cyclic alkyl group that has 3 to 18 carbon atoms and may or
may not be substituted with fluorine, a straight, branched or
cyclic heteroalkyl group that has 3 to 18 carbon atoms and may
or may not be substituted with fluorine, a straight, branched
5 or cyclic alkenyl group that has 3 to 18 carbon atoms and may
or may not be substituted with fluorine, a straight, branched
or cyclic alkynyl group that has 3 to 18 carbon atoms and may
or may not be substituted with fluorine, an alkoxy group that
has 1 to 18 carbon atoms and may or may not be substituted
10 with fluorine, an aryl group that has 5 to 20 carbon atoms and
may or may not be substituted with fluorine, an aralkyl group
that has 5 to 35 carbon atoms and may or may not be
substituted with fluorine, or a heteroaralkyl group that has 5
to 35 carbon atoms and may or may not be substituted with
15 fluorine;

[0194]

with the proviso that at least one of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6
is a substituent represented by the following formula (2b):

[0195]

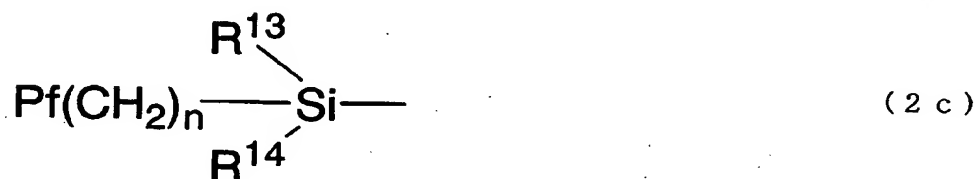


[0196]

(wherein Pf is a straight, branched or cyclic alkyl group that
has 2 to 18 carbon atoms and has all the hydrogen atoms

substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, or a heteroaralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, and n is an integer from 0 to 4.), and/or by the following formula (2c):

[0197]



[0198]

(wherein Pf and n are as defined in the formula (2b) above,

[0199]

R^{13} and R^{14} are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms,

an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, a heteroaralkyl group having 5 to 25 carbon atoms, or a substituent represented by the formula (2b)); and

5 [0200]

the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S).], and subsequently reacting with the reaction product a compound represented by the following formula (10c):

10 [0201]



[0202]

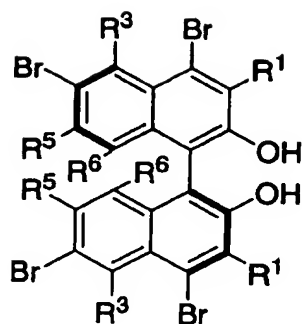
[wherein Pf is a straight, branched or cyclic alkyl group that has 2 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen

atoms substituted with fluorine atoms, a heteroaralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, n is an integer from 0 to 4, and R¹³ and R¹⁴ are each independently a methyl group, an ethyl
5 group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group
10 having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, a heteroaralkyl group having 5 to 25 carbon atoms, or a substituent represented by the formula (2b).]

[0203]

[55] A method for producing the optically active binaphthyl
15 bis-methoxymethyl ether compound according to any of [51] or [52] above represented by the formula (9a), comprising forming a binaphthoxide from an optically active binaphthol compound represented by the following formula (11a) in the presence of an acid-capturing agent or by treatment with a base:

20 [0204]



(1 1 a)

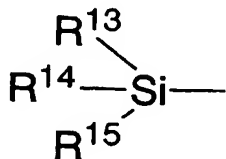
[0205]

[wherein R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a hydrogen atom, a methyl group, an ethyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic heteroalkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxyl group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 35 carbon atoms, or a heteroaralkyl group having 5 to 35 carbon atoms;

[0206]

with the proviso that at least one of R¹, R², R³, R⁴, R⁵, and R⁶ is a substituent represented by the following formula (2a):

[0207]



(2 a)

[0208]

(wherein R^{13} , R^{14} , and R^{15} are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, or a heteroaralkyl group having 5 to 25 carbon atoms); and

[0209]

the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S).], and subsequently reacting the binaphthoxide with chloromethyl ether.

[0210]

[56] A method for stereoselectively producing a compound represented by the following formula (14):

[0219]



[0220]

[wherein R^{16} , R^{17} , R^{18} , R^{19} , and A are as defined above, and the

chiral carbon indicated by an asterisk '*' has an absolute configuration of (R) or (S)], comprising reacting, in a two-phase solution, a Schiff base of a glycine ester or an amide represented by the following formula (12):

5 [0211]



[0212]

[wherein R^{16} and R^{17} are each independently a hydrogen atom or an aryl group that has 5 to 10 carbon atoms and may or may not
10 be substituted with halogen,

[0213]

with the proviso that R^{16} and R^{17} are not a hydrogen atom at the same time;

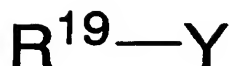
[0214]

15 R^{18} is a straight, branched or cyclic alkyl group having 1 to 6 carbon atoms; and

[0215]

A is an oxygen atom or a nitrogen atom having a single hydrogen atom bound thereto] with an alkyl halide represented
20 by the following formula (13):

[0216]



(13)

[0217]

[wherein R^{19} is a straight, branched or cyclic alkyl group having 1 to 10 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 10 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 10 carbon atoms, or an aralkyl group that has 5 to 25 carbon atoms and may or may not have its nucleus substituted with 1 to 15 halogen atoms; and

10 [0218]

Y is a chlorine atom, a bromine atom, or an iodine atom] in the presence of an optically active quaternary ammonium salt according to [1] to [8] above represented by the formula (1a) or (1b) and an inorganic base.

15 [0221]

[57] The method according to [56] above, wherein the reaction is carried out in a three-phase solution comprising an organic solvent with hydrogen atoms substituted with fluorine atoms, an organic solvent, and water.

20 [0222]

[58] A method for recovering an optically active quaternary ammonium salt, characterized in that an organic solvent, water, a mixed solvent of an organic solvent and water, and/or an

organic solvent with hydrogen atoms substituted with fluorine atoms are/is used to separate the optically active quaternary ammonium salt according to any of claims 5 to 8 represented by the formula (1b) from a product containing the ammonium salt.

5 [0223]

[59] A method for recovering the optically active quaternary ammonium salt according to any of [5] to [8] above represented by the formula (1b), characterized in that, following the production of the compound of the formula (14) by the method according to [56] above, which is carried out in the presence of the optically active quaternary ammonium salt of the formula (1b), the ammonium salt is separated from the reaction mixture containing the optically active quaternary ammonium salt by using an organic solvent, water, a mixed solvent of an organic solvent and water, and/or an organic solvent with hydrogen atoms substituted with fluorine atoms.

[0224]

[60] The method according to [59] above, wherein hexane with its hydrogen atoms substituted with fluorine atoms is used as the fluorine-substituted organic solvent.

ADVANTAGE OF THE INVENTION

[0225]

The axially chiral, optically active spiro-quaternary ammonium salts of the formula (1a) provided in accordance with the present invention can give a high stereoselectivity of 90%

ee or above when used as a phase-transfer catalyst in the asymmetric alkylation of a glycine derivative, and can be applied to a broader range of substrates with high selectivity.

The ammonium salts are advantageous since fewer steps are

involved in the synthesis of the catalysts. Furthermore, when used as a phase-transfer catalyst, the ammonium salts allow the stereoselective production of optically active α -amino acid derivatives, useful intermediates in the synthesis of pharmaceutical or agrochemical products. Because of these advantages, the present invention is of significant importance in industrial applications.

[0226]

The fluorine-containing optically active quaternary ammonium salts of the formula (1b) provided in accordance with the present invention are spiro compounds with a chiral axis and can serve as effective phase-transfer catalysts when used in the asymmetric alkylation of glycine derivatives.

Furthermore, the optically active quaternary ammonium salts can be readily produced, recovered, and purified, and can retain high catalytic activity after they are recycled.

Furthermore, when used as a phase-transfer catalyst, the optically active quaternary ammonium salts allow the stereoselective production of optically active α -amino acid derivatives, useful intermediates in the synthesis of

pharmaceutical or agrochemical products. These advantages

further add to the industrial importance of the present invention.

BEST MODE FOR CARRYING OUT THE INVENTION

[0227]

5 The present invention will now be described in detail.

[0228]

While the optically active quaternary ammonium salt of the present invention shown by the formula (1a) may be any of the compounds defined above, it preferably is a compound in which R^1 and R^7 , R^3 and R^9 , R^4 and R^{10} , R^5 and R^{11} , and R^6 and R^{12} are in each case identical to one another, R^2 and R^8 are identical to one another and are each represented by the formula (2a), and X^- is a fluoride ion, a chloride ion, a bromide ion, an iodide ion, a p-toluenesulfonic acid ion, or a hydroxide ion. Of such compounds, particularly preferred are those in which R^1 , R^3 , R^5 , R^6 , R^7 , R^9 , R^{11} , and R^{12} are each a hydrogen atom, R^2 , R^4 , R^8 , and R^{10} are identical to one another and are each represented by the formula (2a), and X^- is a chloride ion, a bromide ion, an iodide ion, or a p-toluenesulfonic acid ion. Of these, even more preferred are those in which X^- in the formula (1a) is a bromide ion, and R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a

tert-butyl group, an n-octyl group, and a phenyl group.

[0229]

Examples of the compound shown by the formula (1a)

include, but are not limited to, spiro-bis[{(R)-1,1'-bi-{4,6-
5 bis(trimethylsilyl)naphthyl}}-2,2'-dimethyl]ammonium bromide,
spiro-bis[{(R)-1,1'-bi-{4,6-bis(triethylsilyl)naphthyl}}-2,2'-
dimethyl]ammonium bromide, spiro-bis[{(R)-1,1'-bi-{4,6-
bis(tripropylsilyl)naphthyl}}-2,2'-dimethyl]ammonium bromide,
spiro-bis[{(R)-1,1'-bi-{4,6-bis(triisopropylsilyl)naphthyl}}-
10 2,2'-dimethyl]ammonium bromide, spiro-bis[{(R)-1,1'-bi-{4,6-
bis(tributylsilyl)naphthyl}}-2,2'-dimethyl]ammonium bromide,
spiro-bis[{(R)-1,1'-bi-{4,6-bis(triphenylsilyl)naphthyl}}-
2,2'-dimethyl]ammonium bromide, spiro-bis[{(R)-1,1'-bi-{4,6-
bis(dimethyloctylsilyl)naphthyl}}-2,2'-dimethyl]ammonium
15 bromide, spiro-bis[{(R)-1,1'-bi-{4,6-bis(tert-
butyldimethylsilyl)naphthyl}}-2,2'-dimethyl]ammonium bromide,
spiro-bis[{(R)-1,1'-bi-{4,6-
bis(dimethylphenylsilyl)naphthyl}}-2,2'-dimethyl]ammonium
bromide, spiro-bis[{(R)-1,1'-bi-{4,6-bis(tert-
20 butyldiphenylsilyl)naphthyl}}-2,2'-dimethyl]ammonium bromide,
spiro-bis[{(R)-1,1'-bi-{4,6-bis(trimethylsilyl)naphthyl}}-
2,2'-dimethyl]ammonium iodide, spiro-bis[{(R)-1,1'-bi-{4,6-
bis(trimethylsilyl)naphthyl}}-2,2'-dimethyl]ammonium chloride,
spiro-bis[{(R)-1,1'-bi-{4,6-bis(trimethylsilyl)naphthyl}}-
25 2,2'-dimethyl]ammonium fluoride and spiro-bis[{(R)-1,1'-bi-

{4,6-bis(trimethylsilyl)naphthyl}}-2,2'-dimethyl]ammonium
hydroxide, and the corresponding (S)-forms as enantiomers.

[0230]

While the optically active quaternary ammonium salt of
5 the present invention shown by the formula (1b) may be any of
the compounds defined above, it preferably is a compound in
which R^1 and R^7 , R^3 and R^9 , R^4 and R^{10} , R^5 and R^{11} , and R^6 and R^{12}
are in each case identical to one another, R^2 and R^8 are
identical to one another and are each represented by the
10 formula (2c), and X^- is a fluoride ion, a chloride ion, a
bromide ion, an iodide ion, a p-toluenesulfonic acid ion, or a
hydroxide ion. Of such compounds, more preferred are those in
which R^1 , R^3 , R^5 , R^6 , R^7 , R^9 , R^{11} , and R^{12} in the formula (1b) are
each a hydrogen atom, R^2 , R^4 , R^8 , and R^{10} are identical to one
15 another and are each represented by the formula (2c), and X^- is
a chloride ion, a bromide ion, an iodide ion, or a p-
toluenesulfonic acid ion. Of these, most preferred are those
in which X^- in the formula (1b) is a bromide ion, and in the
formula (2c), n is 2, R^{13} and R^{14} are each a methyl group, and
20 Pf is an n-octyl group having all the hydrogen atoms
substituted with fluorine atoms.

[0231]

Examples of the compound shown by the formula (1b)
include, but are not limited to, spiro-bis{(R)-1,1'-bi-[4-(2-
25 perfluorooctylethyl)dimethylsilyl]naphthyl-2,2'-

dimethyl}ammonium bromide, spiro-bis{(R)-1,1'-bi-[6-(2-perfluorooctylethyl)dimethylsilyl]naphthyl-2,2'-

dimethyl}ammonium bromide, spiro-bis{(R)-1,1'-bi-[4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-

5 perfluorooctyl)ethyl]naphthyl-2,2'-dimethyl}ammonium bromide, spiro-bis{(R)-1,1'-bi-[4,6-bis((2-perfluorooctylethyl)dimethylsilyl)]naphthyl-2,2'-

dimethyl}ammonium bromide, spiro-bis{(R)-1,1'-bi-[4,6-bis(-tris(2-perfluorooctylethyl)silyl)]naphthyl-2,2'-

10 dimethyl}ammonium bromide, spiro-bis{(R)-1,1'-bi-[4,6-bis((2-perfluorooctylethyl)dimethylsilyl)]naphthyl-2,2'-

dimethyl}ammonium fluoride, spiro-bis{(R)-1,1'-bi-[4,6-bis((2-perfluorooctylethyl)dimethylsilyl)]naphthyl-2,2'-

dimethyl}ammonium chloride, spiro-bis{(R)-1,1'-bi-[4,6-bis((2-perfluorooctylethyl)dimethylsilyl)]naphthyl-2,2'-

15 dimethyl}ammonium iodide, spiro-bis{(R)-1,1'-bi-[4,6-bis((2-perfluorooctylethyl)dimethylsilyl)]naphthyl-2,2'-

dimethyl}ammonium hydroxide, and spiro-bis{(R)-1,1'-bi-[4,6-bis((2-perfluorooctylethyl)dimethylsilyl)]naphthyl-2,2'-

20 dimethyl}ammonium-4-methylbenzene sulfonate, and the corresponding (S)-forms as enantiomers.

[0232]

While the optically active binaphthyl compound of the present invention shown by the formula (3a) may be any of the
25 compounds defined above, it preferably is a compound in which

R¹, R³, R⁵, and R⁶ are each a hydrogen atom, and R² and R⁴ are identical to one another and are each represented by the formula (2a). Of these, particularly preferred are those in which R¹³, R¹⁴, and R¹⁵ in the formula (2a) are each

5 independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-octyl group, and a phenyl group. Of these compounds, those in which X is a
10 chlorine atom, a bromine atom, an iodine atom, or p-toluenesulfonyloxy group are preferred, with ones in which X is a bromine atom being particularly preferred.

[0233]

Examples of the optically active binaphthyl compound of
15 the present invention shown by the formula (3a) include, but are not limited to, (R)-1,1'-bi-{2-bromomethyl-4,6-bis(trimethylsilyl)}naphthyl, (R)-1,1'-bi-{2-bromomethyl-4,6-bis(triethylsilyl)}naphthyl, (R)-1,1'-bi-{2-bromomethyl-4,6-bis(tripropylsilyl)}naphthyl, (R)-1,1'-bi-{2-bromomethyl-4,6-bis(triisopropylsilyl)}naphthyl, (R)-1,1'-bi-{2-bromomethyl-
20 4,6-bis(tributylsilyl)}naphthyl, (R)-1,1'-bi-{2-bromomethyl-4,6-bis(triphenylsilyl)}naphthyl, (R)-1,1'-bi-{2-bromomethyl-4,6-bis(dimethyloctylsilyl)}naphthyl, (R)-1,1'-bi-{2-bromomethyl-4,6-bis(tert-butyl dimethylsilyl)}naphthyl, (R)-
25 1,1'-bi-{2-bromomethyl-4,6-bis(dimethylphenylsilyl)}naphthyl,

(R)-1,1'-bi-(2-bromomethyl-4,6-bis(tert-butyl-
butyldiphenylsilyl))naphthyl, (R)-1,1'-bi-(2-chloromethyl-4,6-
bis(trimethylsilyl))naphthyl, (R)-1,1'-bi-(2-chloromethyl-4,6-
bis(trimethylsilyl))naphthyl and (R)-1,1'-bi-(2-iodomethyl-
5 4,6-bis(trimethylsilyl))naphthyl, and the corresponding (S)-
forms as enantiomers.

[0234]

The optically active binaphthyl compound of the present
invention shown by the formula (3b) is preferably such that R¹,
10 R³, R⁵, and R⁶ are each a hydrogen atom, and R² and R⁴ are
identical to one another and are each represented by the
formula (2c). Of such compounds, particularly preferred are
those in which X in the formula (3b) is a bromine atom, and in
the formula (2c), n is 2, R¹³ and R¹⁴ are each a methyl group,
15 and Pf is an n-octyl group having all the hydrogen atoms
substituted with fluorine atoms.

[0235]

Examples of the optically active binaphthyl compound of
the present invention shown by the formula (3b) include, but
20 are not limited to, (R)-1,1'-bi-(2-bromomethyl-4-(2-
perfluorooctylethyl)dimethylsilyl)naphthyl, (R)-1,1'-bi-(2-
bromomethyl-6-(2-perfluorooctylethyl)dimethylsilyl)naphthyl,
(R)-1,1'-bi-(2-bromomethyl-4-(2-
perfluorooctylethyl)dimethylsilyl-6-(2-
25 perfluorooctyl)ethyl)naphthyl, (R)-1,1'-bi-(2-bromomethyl-4,6-

bis((2-perfluorooctylethyl)dimethylsilyl)}naphthyl, (R)-1,1'-
bi-{2-bromomethyl-4,6-bis[-tris(2-
perfluorooctylethyl)silyl]}naphthyl, (R)-1,1'-bi-{2-
chloromethyl-4,6-bis[(2-
5 perfluorooctylethyl)dimethylsilyl]}naphthyl, (R)-1,1'-bi-{2-
iodomethyl-4,6-bis((2-
perfluorooctylethyl)dimethylsilyl)}naphthyl and (R)-1,1'-bi-
{2-(4-methylbenzenesulfonyloxy)methyl-4,6-bis[(2-
perfluorooctylethyl)dimethylsilyl]}naphthyl, and the
10 corresponding (S)-forms as enantiomers.
[0236]

The compound of the present invention represented by the
formula (1a) or (1b) can be obtained by reacting the optically
active binaphthyl compound of the formula (3a) or (3b) with
15 ammonia. The ammonia used may be a 10wt% to saturated aqueous
ammonia and preferably a 20 to 28wt% aqueous ammonia. Water or
an organic solvent inert to the reaction may be added as a
solvent. The reaction is preferably carried out in a sealed
condition to avoid loss of ammonia. The amount of ammonia used
20 is typically 1 to 8 equivalents, and preferably 2 to 5
equivalents, relative to the substrate used. The reaction is
typically carried out at a temperature of 5°C to 30°C and at a
substrate concentration of 5 to 20wt%, and is carried out over
a time period of typically 5 to 72 hours, and preferably 10 to
25 36 hours. In this manner, the desired ammonium salt can be

obtained in high yield.

[0237]

While the optically active binaphthyl dihydroxy compound of the present invention shown by the formula (4a) may be any of the compounds defined above, it preferably is a compound in which R^1 , R^3 , R^5 , and R^6 are each a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2a). Of these, particularly preferred are those in which R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-octyl group, and a phenyl group.

[0238]

Examples of the optically active binaphthyl dihydroxy compound of the present invention shown by the formula (4a) include, but are not limited to, (R)-1,1'-bi-{4,6-bis(trimethylsilyl)-2-hydroxymethyl}naphthyl, (R)-1,1'-bi-{4,6-bis(triethylsilyl)-2-hydroxymethyl}naphthyl, (R)-1,1'-bi-{4,6-bis(tripropylsilyl)-2-hydroxymethyl}naphthyl, (R)-1,1'-bi-{4,6-bis(triisopropylsilyl)-2-hydroxymethyl}naphthyl, (R)-1,1'-bi-{4,6-bis(tributylsilyl)-2-hydroxymethyl}naphthyl, (R)-1,1'-bi-{4,6-bis(triphenylsilyl)-2-hydroxymethyl}naphthyl, (R)-1,1'-bi-{4,6-bis(dimethyloctylsilyl)-2-

hydroxymethyl)naphthyl, (R)-1,1'-bi-{4,6-bis(tert-butyl-
butyldimethylsilyl)-2-hydroxymethyl)naphthyl, (R)-1,1'-bi-
{4,6-bis(dimethylphenylsilyl)-2-hydroxymethyl)naphthyl and
(R)-1,1'-bi-{4,6-bis(tert-butyl-diphenylsilyl)-2-
5 hydroxymethyl)naphthyl, and the corresponding (S)-forms as
enantiomers.

[0239]

The optically active binaphthyl dihydroxy compound of the
present invention shown by the formula (4b) is preferably such
10 that R^1 , R^3 , R^5 , and R^6 are each a hydrogen atom, and R^2 and R^4
are identical to one another and are each represented by the
formula (2c). Of such compounds, most preferred are those in
which in the formula (2c), R^{13} and R^{14} are each a methyl group,
Pf is an n-octyl group having all the hydrogen atoms
15 substituted with fluorine atoms, and n is 2.

[0240]

Examples of the optically active binaphthyl dihydroxy
compound of the present invention shown by the formula (5)
include (R)-1,1'-bi-{2-hydroxymethyl-4-(2-
20 perfluorooctylethyl)dimethylsilyl)naphthyl, (R)-1,1'-bi-{2-
hydroxymethyl-6-(2-perfluorooctylethyl)dimethylsilyl)naphthyl,
(R)-1,1'-bi-{2-hydroxymethyl-4-(2-
perfluorooctylethyl)dimethylsilyl-6-(2-
perfluorooctyl)ethyl)naphthyl, (R)-1,1'-bi-{2-hydroxymethyl-
25 4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]}naphthyl and

(R)-1,1'-bi-{2-hydroxymethyl-4,6-bis[-tris(2-perfluorooctylethyl)silyl]}naphthyl, and the corresponding (S)-forms as enantiomers.

[0241]

5 The optically active binaphthyl compound of the present invention represented by the formula (3a) or (3b) can be obtained as follows: For example, when it is desired to produce a halogenated product, the optically active binaphthyl dihydroxy compound of the formula (4a) or (4b) is reacted with
10 triphenylphosphine, and carbon tetrabromide or carbon tetrachloride in a proper solvent such as tetrahydrofuran. The reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically -10°C to 50°C, and preferably 10°C to 30°C, and is carried out over
15 a time period of typically 10 minutes to 10 hours, and preferably 1 hour to 5 hours. In this manner, the desired dihalogenated product can be obtained in high yield. When it is desired to produce a sulfonyloxy product, the optically active binaphthyl dihydroxy compound (4a) or (4b) is reacted
20 with p-toluenesulfonyl chloride in a proper solvent such as dichloromethane and in the presence of an acid-capturing agent such as triethylamine. The reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically -40°C to 20°C, and preferably -10°C
25 to 10°C, and is carried out over a time period of typically 10

minutes to 10 hours, and preferably 1 hour to 5 hours. In this manner, the desired sulfonyloxy product can be obtained in high yield.

[0242]

5 While the optically active binaphthyl diester compound of the present invention shown by the formula (5a) may be any of the compounds defined above, it preferably is a compound in which R^1 , R^3 , R^5 , and R^6 are each a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the
10 formula (2a). Of these, particularly preferred are those in which R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-
15 butyl group, a tert-butyl group, an n-octyl group, and a phenyl group.

[0243]

 Examples of the optically active binaphthyl diester compound of the present invention shown by the formula (5a)
20 include (R)-1,1'-bi-{4,6-bis(trimethylsilyl)-2-methoxycarbonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(triethylsilyl)-2-methoxycarbonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(tripropylsilyl)-2-methoxycarbonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(triisopropylsilyl)-2-methoxycarbonyl}naphthyl, (R)-
25 1,1'-bi-{4,6-bis(tributylsilyl)-2-methoxycarbonyl}naphthyl,

(R)-1,1'-bi-{4,6-bis(triphenylsilyl)-2-methoxycarbonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(dimethyloctylsilyl)-2-methoxycarbonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(tert-butyldimethylsilyl)-2-methoxycarbonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(dimethylphenylsilyl)-2-methoxycarbonyl}naphthyl and (R)-1,1'-bi-{4,6-bis(tert-butyldiphenylsilyl)-2-methoxycarbonyl}naphthyl, and the corresponding (S)-forms as enantiomers.

10 [0244]

The optically active binaphthyl diester compound of the present invention shown by the formula (5b) is preferably such that R^1 , R^3 , R^5 , and R^6 are each a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2c). Of such compounds, particularly preferred are those in which in the formula (2c), R^{13} and R^{14} are each a methyl group, Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms, and n is 2.

[0245]

20 Examples of the optically active binaphthyl diester compound of the present invention shown by the formula (5b) include, but are not limited to, (R)-1,1'-bi-{2-methoxycarbonyl-4-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-methoxycarbonyl-6-(2-

25

perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-methoxycarbonyl-4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-perfluorooctyl)ethyl}naphthyl, (R)-1,1'-bi-{2-methoxycarbonyl-4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]}naphthyl and
5 (R)-1,1'-bi-{2-methoxycarbonyl-4,6-bis[-tris(2-perfluorooctylethyl)silyl]}naphthyl, and the corresponding (S)-forms as enantiomers.

[0246]

The optically active binaphthyl dihydroxy compound of the
10 present invention represented by the formula (4a) or (4b) can be obtained, for example, by reacting the optically active binaphthyl diester compound of the formula (5a) or (5b) with a hydrogen anion such as LiAlH_4 in a proper solvent such as tetrahydrofuran. The reaction is carried out at a substrate
15 concentration of typically 5 to 30wt% and at a temperature of typically -20°C to 30°C , and preferably -10°C to 10°C , and is carried out over a time period of typically 10 minutes to 5 hours, and preferably 20 minutes to 2 hours. In this manner, the desired dihydroxyl methyl product can be obtained in high
20 yield.

[0247]

While the optically active binaphthyl compound of the present invention shown by the formula (6a) may be any of the compounds defined above, it preferably is a compound in which
25 R^1 , R^3 , R^5 , and R^6 are each a hydrogen atom, and R^2 and R^4 are

identical to one another and are each represented by the formula (2a). Of these, particularly preferred are those in which R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-octyl group, and a phenyl group.

[0248]

Examples of the optically active binaphthyl compound of the present invention shown by the formula (6a) include, but are not limited to, (R)-1,1'-bi-{4,6-bis(trimethylsilyl)-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(triethylsilyl)-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(tripropylsilyl)-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(triisopropylsilyl)-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(tributylsilyl)-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(triphenylsilyl)-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(dimethyloctylsilyl)-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(tert-butyl dimethylsilyl)-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4,6-bis(dimethylphenylsilyl)-2-trifluoromethanesulfonyl}naphthyl and (R)-1,1'-bi-{4,6-

bis(tert-butyldiphenylsilyl)-2-trifluoromethanesulfonyl}naphthyl, and the corresponding enantiomers, or (S)-forms.

[0249]

5 The optically active binaphthyl compound of the present invention shown by the formula (6b) is preferably such that R^1 , R^3 , R^5 , and R^6 are each a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2c). Of such compounds, particularly preferred are
10 those in which in the formula (2c), R^{13} and R^{14} are each a methyl group, Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms, and n is 2.

[0250]

Examples of the optically active binaphthyl compound of
15 the present invention shown by the formula (6b) include (R)-1,1'-bi-{4-(2-perfluorooctylethyl)dimethylsilyl-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{6-(2-perfluorooctylethyl)dimethylsilyl-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-perfluorooctyl)ethyl-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]-2-trifluoromethanesulfonyl}naphthyl and (R)-1,1'-bi-{4,6-bis[tris(2-perfluorooctylethyl)silyl]-2-trifluoromethanesulfonyl}naphthyl, and the corresponding (S)-
25

forms as enantiomers.

[0251]

The optically active binaphthyl dimethyl ester compound of the present invention represented by the formula (5a) or (5b) can be obtained, for example, by reacting the optically active binaphthyl compound of the formula (6a) or (6b) with carbon monoxide and methanol in a proper solvent such as dimethyl sulfoxide in the presence of a palladium catalyst and an organic base, such as diisopropylethylamine, for capturing an acid, in a carbon monoxide atmosphere, which may be pressurized. The reaction is carried out at a substrate concentration of typically 5 to 30wt% under a pressure of typically 1 to 30atm, and preferably 5 to 20atm, and at a temperature of typically room temperature to 200°C, and preferably 80°C to 130°C, and is typically carried out over a time period of 24 to 72 hours. The palladium catalyst may have no valency or it may be prepared in the reaction system from a divalent acetate or the like. The palladium catalyst is typically used in an amount of 5 to 20mol% relative to the substrate. The base is used in an amount of typically 2 to 8 equivalents, and preferably 2.5 to 5 equivalents, relative to the substrate. Methanol is used in an amount of 2 to 200 equivalents, and preferably 10 to 50 equivalents, relative to the substrate. In this manner, the desired diester product can be obtained in high yield.

[0252]

While the optically active binaphthol compound of the present invention shown by the formula (7a) may be any of the compounds defined above, it preferably is a compound in which

5 R^1 , R^3 , R^5 , and R^6 are each a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2a). Of these, most preferred are those in which R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl
10 group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-octyl group, and a phenyl group.

[0253]

Examples of the optically active binaphthol compound of the present invention shown by the formula (7a) include, but
15 are not limited to, (R)-1,1'-bi-{4,6-bis(trimethylsilyl)-2-hydroxy}naphthyl, (R)-1,1'-bi-{4,6-bis(triethylsilyl)-2-hydroxy}naphthyl, (R)-1,1'-bi-{4,6-bis(tripropylsilyl)-2-hydroxy}naphthyl, (R)-1,1'-bi-{4,6-bis(triisopropylsilyl)-2-hydroxy}naphthyl, (R)-1,1'-bi-{4,6-bis(tributylsilyl)-2-hydroxy}naphthyl, (R)-1,1'-bi-{4,6-bis(triphenylsilyl)-2-hydroxy}naphthyl, (R)-1,1'-bi-{4,6-bis(dimethyloctylsilyl)-2-hydroxy}naphthyl, (R)-1,1'-bi-{4,6-bis(tert-butyl-
20 dimethylsilyl)-2-hydroxy}naphthyl, (R)-1,1'-bi-{4,6-bis(dimethylphenylsilyl)-2-hydroxy}naphthyl and (R)-1,1'-bi-

{4,6-bis(*tert*-butyldiphenylsilyl)-2-hydroxy}naphthyl, and the corresponding (S)-forms as enantiomers.

[0254]

The optically active binaphthol compound of the present invention shown by the formula (7b) is preferably such that R¹, R³, R⁵, and R⁶ are each a hydrogen atom, and R² and R⁴ are identical to one another and are each represented by the formula (2c). Of such compounds, particularly preferred are those in which R¹³ and R¹⁴ are each a methyl group, Pf is an n-octyl group with all the hydrogen atoms substituted with fluorine atoms, and n is 2 in the formula (2c).

[0255]

Specific examples of the optically active binaphthol compound of the present invention shown by the formula (7b) include (R)-1,1'-bi-{2-hydroxy-4-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-hydroxy-6-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-hydroxy-4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-perfluorooctyl)ethyl}naphthyl, (R)-1,1'-bi-{2-hydroxy-4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]}naphthyl and (R)-1,1'-bi-{2-hydroxy-4,6-bis[-tris(2-perfluorooctylethyl)silyl]}naphthyl, and the corresponding (S)-forms as enantiomers.

[0256]

The optically active binaphthyl compound of the present

invention represented by the formula (6a) or (6b) can be obtained, for example, by reacting the optically active binaphthol compound of the formula (7a) or (7b) with a triflating agent, such as a trifluoromethanesulfonic acid

5 anhydride or trifluoromethanesulfonyl chloride, in an inert solvent such as dichloromethane in the presence of an organic base such as triethylamine. The reaction is typically carried out at a substrate concentration of 5 to 30wt% and at a temperature of -78°C to room temperature, and is typically
10 carried out over a time period of 30 minutes to 3 hours. In this manner, the desired ditriflate product can be obtained in high yield.

[0257]

While the optically active binaphthyl bis-methoxymethyl
15 ether compound of the present invention shown by the formula (8a) may be any of the compounds defined above, it preferably is a compound in which R^1 , R^3 , R^5 , and R^6 are each a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2a). Of these, most preferred are
20 those in which R^{13} , R^{14} , and R^{15} in the formula (2a) are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-octyl group, and a
25 phenyl group.

[0258]

Examples of the optically active binaphthyl diether compound of the present invention shown by the formula (8a) include, but are not limited to, (R)-1,1'-bi-{4,6-bis(trimethylsilyl)-2-methoxymethoxy}naphthyl, (R)-1,1'-bi-{4,6-bis(triethylsilyl)-2-methoxymethoxy}naphthyl, (R)-1,1'-bi-{4,6-bis(tripropylsilyl)-2-methoxymethoxy}naphthyl, (R)-1,1'-bi-{4,6-bis(triisopropylsilyl)-2-methoxymethoxy}naphthyl, (R)-1,1'-bi-{4,6-bis(tributylsilyl)-2-methoxymethoxy}naphthyl, (R)-1,1'-bi-{4,6-bis(triphenylsilyl)-2-methoxymethoxy}naphthyl, (R)-1,1'-bi-{4,6-bis(dimethyloctylsilyl)-2-methoxymethoxy}naphthyl, (R)-1,1'-bi-{4,6-bis(*tert*-butyldimethylsilyl)-2-methoxymethoxy}naphthyl, (R)-1,1'-bi-{4,6-bis(dimethylphenylsilyl)-2-methoxymethoxy}naphthyl and (R)-1,1'-bi-{4,6-bis(*tert*-butyldiphenylsilyl)-2-methoxymethoxy}naphthyl, and the corresponding (S)-forms as enantiomers.

[0259]

The optically active binaphthyl bis-methoxymethyl ether compound of the present invention shown by the formula (8b) is preferably such that R^1 , R^3 , R^5 , and R^6 are each a hydrogen atom, and R^2 and R^4 are identical to one another and are each represented by the formula (2c). Of such compounds, particularly preferred are those in which in the formula (2c), R^{13} and R^{14} are each a methyl group, Pf is an n-octyl group

having all the hydrogen atoms substituted with fluorine atoms,
and n is 2.

[0260]

Examples of the optically active binaphthyl bis-

5 methoxymethyl ether compound of the present invention shown by
the formula (8b) include, but are not limited to, (R)-1,1'-bi-
{2-methoxymethoxy-4-(2-
perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-
methoxymethoxy-6-(2-perfluorooctylethyl)dimethylsilyl}naphthyl,
10 (R)-1,1'-bi-{2-methoxymethoxy-4-(2-
perfluorooctylethyl)dimethylsilyl-6-(2-
perfluorooctyl)ethyl}naphthyl, (R)-1,1'-bi-{2-methoxymethoxy-
4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]}naphthyl and
(R)-1,1'-bi-{2-methoxymethoxy-4,6-bis[-tris(2-
15 perfluorooctylethyl)silyl]}naphthyl, and the corresponding
(S)-forms as enantiomers.

[0261]

The optically active binaphthol compound of the present
invention represented by the formula (7a) or (7b) can be
20 obtained, for example, by reacting the optically active
binaphthyl bis-methoxymethyl ether compound of the formula
(8a) or (8b) with an organic acid, such as p-toluenesulfonic
acid, in a proper solvent, such as dichloromethane and
methanol, or a mixed solvent. Preferably, the organic acid is
25 used in an amount of 2 to 3 equivalents relative to the

substrate. The reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically 10°C to 80°C, preferably 30°C to 60°C, and is carried out over a time period of typically 20 minutes to 48 hours, and preferably 2 hours to 24 hours. In this manner, the desired binaphthol product can be obtained in high yield.

[0262]

The optically active binaphthyl bis-methoxymethyl ether compound of the present invention represented by the formula (8a) can be obtained, for example, as follows: The optically active binaphthyl diether compound of the formula (9a) is reacted with butyl lithium in a proper solvent, such as tetrahydrofuran, to replace the bromine atoms with lithium atoms. The reaction product is then reacted with the silyl chloride of the formula (10a) above, a compound represented by the following formula (10b):

[0263]



[0264]

(wherein Pf and n are as defined in the formula (2b) above), or the silyl chloride of the formula (10c) above. Using the alkyl lithium in an amount of typically 8 to 12 equivalents relative to the substrate, the reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a

temperature of typically -100°C to -50°C , and preferably -85°C to -75°C , and is carried out over a time period of typically 20 minutes to 3 hours, and preferably 30 minutes to 2 hours. In this manner, the desired lithio product can be obtained. To
5 this product, the alkyl silyl chloride is added, at the same temperature, in an amount of 4 to 8 equivalents relative to the substrate, and the reaction is carried out at a temperature of typically -80°C to 30°C , and preferably 0°C to room temperature, over a time period of typically 20 minutes
10 to 2 hours, and preferably 30 minutes to 1 hour. In this manner, the desired product can be obtained in high yield.
[0265]

While the optically active binaphthyl bis-methoxymethyl ether compound of the present invention shown by the formula
15 (9a) or (9b) may be any of the compounds defined above, it preferably is a compound in which R^1 , R^3 , R^5 and R^6 are each a hydrogen atom.
[0266]

While the silyl chloride of the present invention shown
20 by the formula (10a) may be any of the compounds defined above, compounds are particularly preferred in which R^{13} , R^{14} , and R^{15} are each independently a substituent selected from the group consisting of a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group,
25 a sec-butyl group, a tert-butyl group, an n-octyl group, and a

phenyl group.

[0267]

While the silyl chloride of the present invention shown by the formula (10c) may be any of the compounds defined above, 5 compounds are particularly preferred in which R^{13} and R^{14} are each a methyl group, Pf is an n-octyl group with all the hydrogen atoms substituted with fluorine atoms, and n is 2 in the formula (2c).

[0268]

10 The compound of the present invention represented by the formula (9a) can be obtained, for example, by reacting the compound of the formula (11a) with sodium hydride in a solvent, such as tetrahydrofuran, to form an alkoxide, followed by addition of chloromethylmethyl ether. The reaction is carried 15 out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically -40°C to room temperature, and preferably -10°C to 0°C , and is carried out over a time period of typically 20 minutes to 3 hours, and preferably 30 minutes to 2 hours. In this manner, the desired product can be 20 obtained in high yield. Of the compounds shown by the formula (9a), those in which R^1 , R^3 , R^5 , and R^6 are each a hydrogen atom can be synthesized according to the process described in *J. Org. Chem.*, 2001, 66, 2358.

[0269]

25 The compound of the present invention represented by the

formula (9b) can be obtained by reacting a corresponding binaphthol product with sodium hydride in a solvent, such as tetrahydrofuran, to form an alkoxide, followed by addition of chloromethylmethyl ether. The reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically -40°C to room temperature, and preferably -10°C to 0°C, and is carried out over a time period of typically 20 minutes to 3 hours, and preferably 30 minutes to 2 hours. In this manner, the desired product can be obtained in high yield.

[0270]

According to the present invention, the optically active quaternary ammonium salt of the formula (1a) or (1b) is used as a chiral phase-transfer catalyst.

[0271]

In the stereoselective production of the compound of the formula (14), a Schiff base of a glycine ester shown by the formula (12) is asymmetrically alkylated with a halogenated alkyl of the formula (13) in a two-phase solvent system using the optically active quaternary ammonium salt of the formula (1a) or (1b) as a phase-transfer catalyst. The solvent used is a mixture of a water-immiscible hydrocarbon solvent, such as toluene, and a 40 to 60wt% aqueous solution of an alkaline metal, such as potassium hydroxide and cesium hydroxide, with the ratio of the organic phase to the aqueous phase being in

the range of 5:1 to 1:3, preferably, 5:1 to 1:1. This reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically -40°C to 10°C, and preferably -25°C to 5°C, and is carried out over a time period of typically 1 hour to 200 hours, and preferably 5 hours to 180 hours. The amount of the phase-transfer catalyst used is in the range of 0.2 to 2mol%, and preferably in the range of 0.8 to 1.2mol% relative to the substrate. In this manner, the desired optically active α -amino acid derivative can be obtained in high yield in a highly stereoselective manner.

[0272]

In the above-describe process, the reaction product shown by the formula (16) is given as an (S)-form when the axially chiral, optically active quaternary ammonium salt of the formula (1a) or (1b) to serve as the phase-transfer catalyst has an absolute configuration of (R, R). Conversely, the product is given as an (R)-form when the catalyst has an absolute configuration of (S, S).

[0273]

According to the present invention, the above-described process may be carried out in a three-phase solvent system comprising an organic solvent with the hydrogen atoms substituted with fluorine atoms, an organic solvent and water. The organic solvent with the hydrogen atoms substituted with fluorine atoms may be a fluorous solvent. Examples of fluorous

solvent are perfluorinated alkanes and cycloalkanes, such as perfluorohexane and perfluoromethylcyclohexane. The fluorous solvent is added in an amount of 0.1 to 1.0 times by volume of the organic solvent used.

5 [0274]

According to the present invention, the optically active quaternary ammonium salt of the formula (1b) can be recovered after it has been used in the reaction as a catalyst.

[0275]

10 The ammonium salt can be recovered by using any proper technique: For example, it can be readily recovered by using an organic solvent, water, a mixed solvent of an organic solvent and water and/or an organic solvent with the hydrogen atoms substituted with fluorine atoms, to separate the
15 optically active quaternary ammonium salt of the formula (1b) from a product (e.g., the reaction mixture of the above-described reaction) containing the ammonium salt. When necessary, the reaction mixture is diluted with water and an organic solvent, such as toluene, and is then subjected to
20 separation with a fluorous solvent, such as perfluorinated alkanes and cycloalkanes, including perfluorohexane and perfluoromethylcyclohexane. In this manner, only the catalyst can be recovered from the fluorous layer in high yield.

[0276]

25 According to the present invention, the recovered

catalyst can be purified by removing the fluorous solvent from the fluorous solution by distillation, and subjecting the residue to a silica gel column chromatography using a relatively high polar organic solvent, such as a mixed solvent of dichloromethane/methanol, as an eluant. The crude recovered product obtained by concentrating the fluorous solvent may be directly used as a catalyst in the subsequent reaction.

Examples

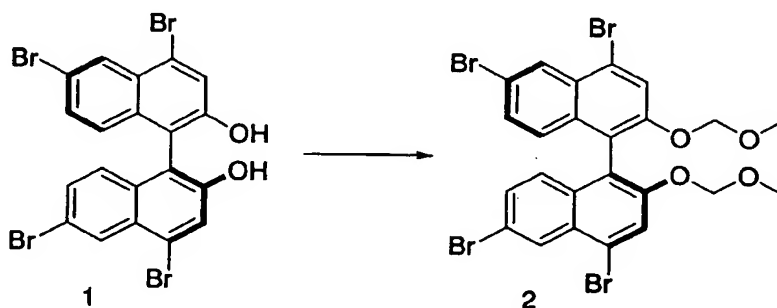
[0277]

The present invention will now be described in further detail with reference to examples of axially chiral, optically active spiro-quaternary ammonium salts represented by the formula (1a). These examples, however, are provided by way of example only and are not intended to limit the scope of the invention in any way.

[0278]

Example 1 Synthesis of (R)-1,1'-bi-(4,6-dibromo-2-methoxymethoxy)naphthyl (2)

[0279]



[0280]

In an argon atmosphere, 60% sodium hydride (0.880 g, 22 mmol) was added to a tetrahydrofuran solution (50 mL) of Compound 1 (6.02 g, 10 mmol) at 0°C and the mixture was stirred for 10 minutes. Subsequently, chloromethyl ether (1.67 mL, 22 mmol) was added at 0°C, and the reaction mixture was allowed to warm to room temperature and was then stirred for 1 hour. After completion of the reaction, the reaction mixture was poured into water and was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. To the resulting white solid, hexane (30 mL) was added and the solution was filtered to give Compound 2 (6.90 g, 10 mmol) in a quantitative manner.

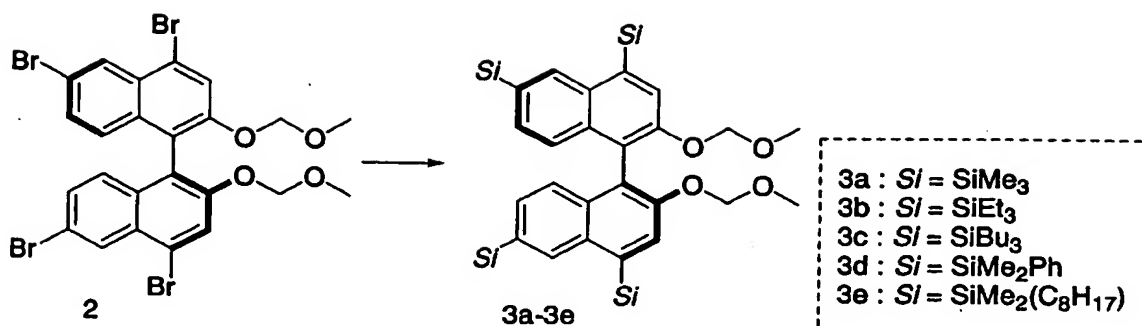
[0281]

¹H-NMR (400 MHz, CDCl₃) δ 8.43 (2H, d, J = 2.4 Hz, Ar-H), 7.94 (2H, s, Ar-H), 7.33 (2H, dd, J = 2.4 Hz, 9.2 Hz, Ar-H), 6.96 (2H, d, J = 9.2 Hz, Ar-H), 5.07 (2H, d, J = 7.2 Hz, Ar-OCH₂), 4.98 (2H, d, J = 7.2 Hz, Ar-OCH₂), 3.20 (6H, s, OCH₃).

[0282]

Examples 2 through 6 Synthesis of (R)-1,1'-bi-(4,6-bis(trialkylsilyl)-2-methoxymethoxy)naphthyls (3a through 3e)

[0283]



[0284]

In an argon atmosphere, a 1.40M *tert*-butyllithium solution (1.93 mL, 2.7 mmol) was added dropwise to a

5 tetrahydrofuran solution (10 mL) of Compound 2 (0.207 g, 0.30 mmol) at -78°C, and the mixture was stirred for 15 minutes. Subsequently, a corresponding trialkylchlorosilane (1.80 mmol) was added at -78°C, and the reaction mixture was allowed to warm to room temperature and was then stirred for 4 hours.

10 After completion of the reaction, the reaction mixture was poured into water and was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. The

15 resulting residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of diethylether/hexane to give Compounds 3a through 3e in yields of 60 to 85%.

[0285]

Chemical data for the products of Examples 2 through 6

20 are shown below.

[0286]

<Product of Example 2 (Compound 3a)>

(R)-1,1'-bi-{4,6-bis(trimethylsilyl)-2-

methoxymethoxy}naphthyl: ¹H-NMR (400 MHz, CDCl₃) σ 8.29 (2H, s,

5 Ar-H), 7.72 (2H, s, Ar-H), 7.31 (2H, dd, J = 1.2 Hz, 8.4 Hz,

Ar-H), 7.16 (2H, d, J = 8.4 Hz, Ar-H), 5.03 (2H, d, J = 6.4 Hz,

Ar-OCH₂), 4.95 (2H, d, J = 6.4 Hz, Ar-OCH₂), 3.15 (6H, s, OCH₃),

0.55 (18H, s, SiCH₃), 0.27 (18 H, s, SiCH₃).

[0287]

10 <Product of Example 3 (Compound 3b)>

(R)-1,1'-bi-{4,6-bis(triethylsilyl)-2-methoxymethoxy}naphthyl:

¹H-NMR (400 MHz, CDCl₃) σ 8.24 (2H, s, Ar-H), 7.67 (2H, s, Ar-

H), 7.31 (2H, dd, J = 1.2 Hz, 8.4 Hz, Ar-H), 7.19 (2H, d, J =

8.4 Hz, Ar-H), 5.04 (2H, d, J = 6.4 Hz, Ar-OCH₂), 4.91 (2H, d,

15 J = 6.4 Hz, Ar-OCH₂), 2.97 (6H, s, OCH₃), 1.40-0.80 (60H, m,

SiCH₂CH₃).

[0288]

<Product of Example 4 (Compound 3c)>

(R)-1,1'-bi-{4,6-bis(tributylsilyl)-2-methoxymethoxy}naphthyl:

20 ¹H-NMR (400 MHz, CDCl₃) σ 8.25 (2H, s, Ar-H), 7.64 (2H, s, Ar-

H), 7.31 (2H, d, J = 8.4 Hz, Ar-H), 7.21 (2H, d, J = 8.4 Hz,

Ar-H), 5.04 (2H, d, J = 6.4 Hz, Ar-OCH₂), 4.89 (2H, d, J = 6.4

Hz, Ar-OCH₂), 2.89 (6H, s, OCH₃), 1.39-0.80 (108H, m,

SiCH₂CH₂CH₂CH₃).

25 [0289]

<Product of Example 5 (Compound 3d)>

(R)-1,1'-bi-{4,6-bis(dimethylphenylsilyl)-2-methoxymethoxy}naphthyl: ¹H-NMR (400 MHz, CDCl₃) σ 8.05 (2H, s, Ar-H), 7.33 (2H, s, Ar-H), 7.59-7.28 (22H, m, Ar-H), 7.10 (2H, d, J = 8.4 Hz, Ar-H), 5.97 (2H, d, J = 6.4 Hz, Ar-OCH₂), 4.88 (2H, d, J = 6.4 Hz, Ar-OCH₂), 3.04 (6H, s, OCH₃), 0.67 (12H, s, SiCH₃), 0.41 (12H, s, SiCH₃).

[0290]

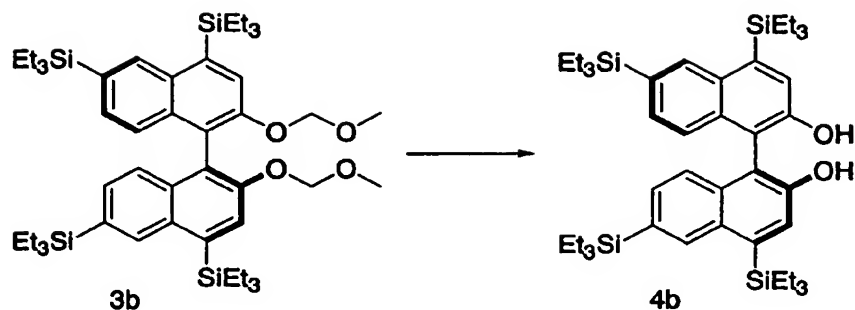
<Product of Example 6 (Compound 3e)>

(R)-1,1'-bi-{4,6-bis(dimethyloctylsilyl)-2-methoxymethoxy}naphthyl: ¹H-NMR (400 MHz, CDCl₃) σ 8.27 (2H, s, Ar-H), 7.70 (2H, s, Ar-H), 7.30 (2H, dd, J = 1.2 Hz, 8.4 Hz, Ar-H), 7.16 (2H, d, J = 8.4 Hz, Ar-H), 5.03 (2H, d, J = 6.4 Hz, Ar-OCH₂), 4.93 (2H, d, J = 6.4 Hz, Ar-OCH₂), 3.09 (6H, s, OCH₃), 1.45-0.72 (68H, m, SiC₈H₁₇), 0.48 (12H, s, SiCH₃), 0.27 (12H, s, SiCH₃).

[0291]

Example 7 Synthesis of (R)-1,1'-bi-{4,6-bis(triethylsilyl)-2-hydroxy}naphthyl (4b)

[0292]



[0293]

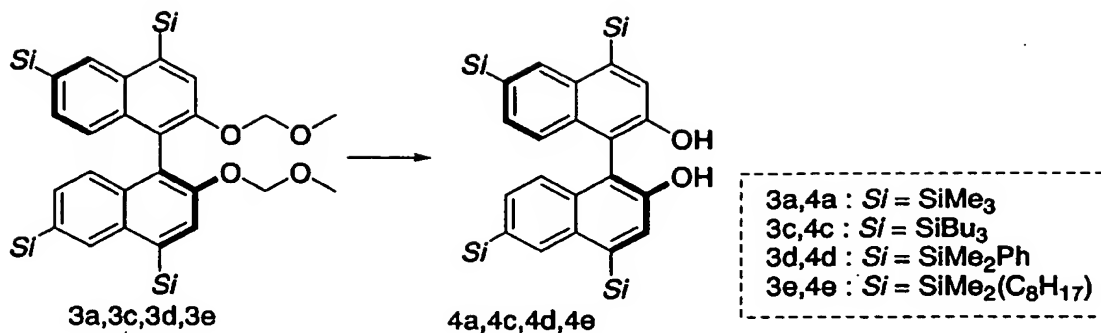
p-toluenesulfonic acid monohydrate (0.114g, 0.60 mmol) was added to Compound 3b (0.30 mmol) in dichloromethane (10 mL) and methanol (10 mL) at room temperature, and the mixture was stirred at 50°C for 24 hours. After completion of the reaction, the reaction mixture was poured into water and was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure to give Compound 4b in a quantitative yield.

[0294]

$^1\text{H-NMR}$ (400 MHz, CDCl_3) σ 8.28 (2H, s, Ar-H), 7.54 (2H, s, Ar-H), 7.39 (2H, dd, $J = 1.2$ Hz, 8.4 Hz, Ar-H), 7.29 (2H, d, $J = 8.4$ Hz, Ar-H), 4.99 (2H, s, OH), 1.11-0.80 (60H, m, SiCH_2CH_3).

Examples 8 through 11 Synthesis of (R)-1,1'-bi-{4,6-bis(trialkylsilyl)-2-hydroxy}naphthyls (4a, 4c, 4d, and 4e)

[0295]



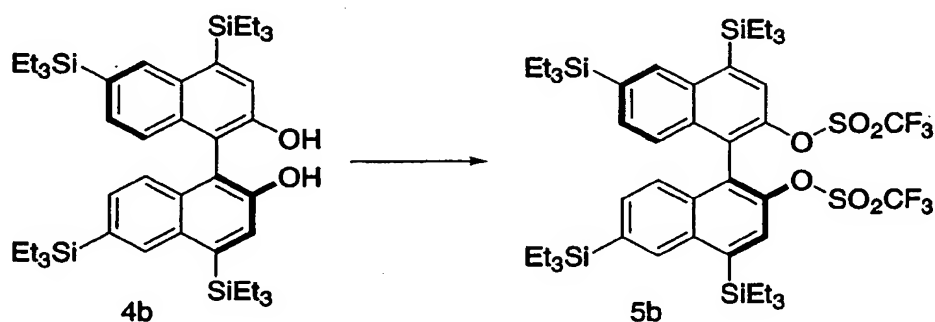
[0296]

To obtain Compounds 4a, 4c, 4d, and 4e in quantitative yields, the same procedure was followed as in Example 7, except that Compound 3a, 3c, 3d, or 3e was used as the starting material in place of Compound 3b.

[0297]

Example 12 Synthesis of (R)-1,1'-bi-(4,6-bis(triethylsilyl)-2-trifluoromethanesulfonylnaphthyl (5b)

10 [0298]



[0299]

In an argon atmosphere, triethylamine (11.1 mmol) was added to a dichloromethane solution (25 mL) of Compound 4b (3.70 mmol), and the mixture was cooled to -78°C.

Trifluoromethanesulfonic acid anhydride (11.1 mmol) was added dropwise, and the mixture was allowed to warm to room temperature, followed by stirring for 1 hour. Subsequently, the reaction mixture was poured into a saturated aqueous

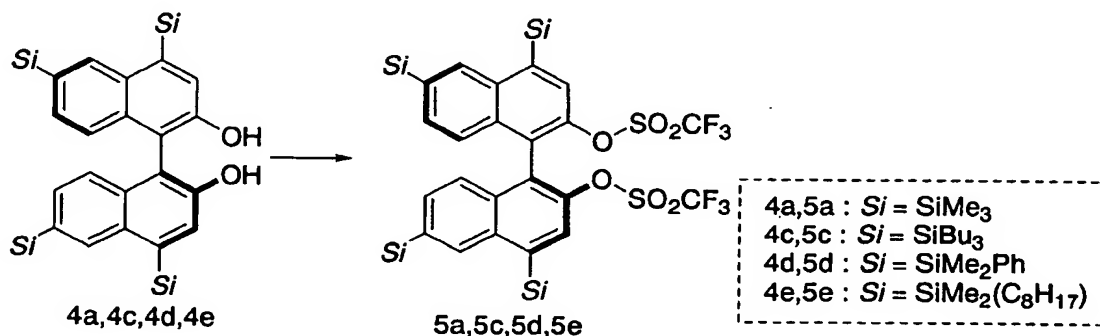
5 solution of ammonium chloride and the solution was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the resulting residue was subjected to a silica gel column chromatography and eluted
10 with a mixed solvent of diethylether/hexane to give Compound 5b in a quantitative yield.

[0300]

$^1\text{H-NMR}$ (400MHz, CDCl_3) δ 8.35 (2H, s, Ar-H), 7.71 (2H, s, Ar-H), 7.47 (2H, dd, $J = 1.2$ Hz, 8.4 Hz, Ar-H), 7.30 (2H, d, $J = 8.4$
15 Hz, Ar-H), 1.11-0.85 (60H, m, SiCH_2CH_3).

Examples 13 through 16 Synthesis of (R)-1,1'-bi-{4,6-bis(trialkylsilyl)-2-trifluoromethanesulfonyl}naphthyls (5a, 5c, 5d, and 5e)

[0301]



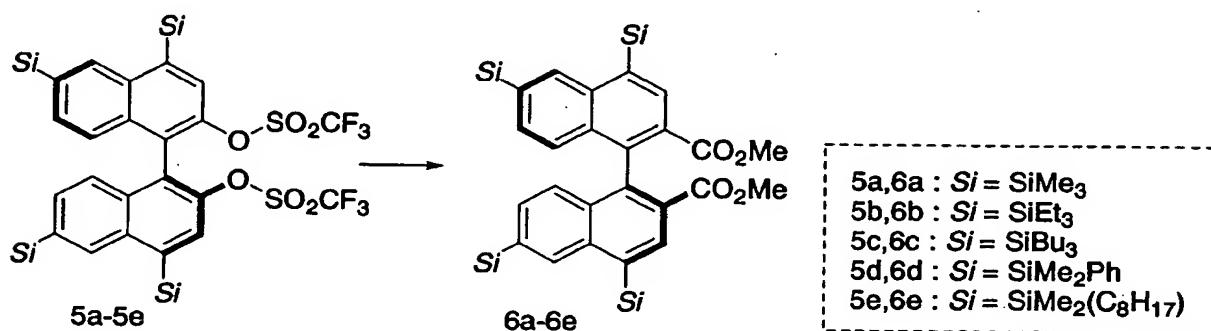
[0302]

To obtain Compounds 5a, 5c, 5d, and 5e in quantitative yields, the same procedure was followed as in Example 12, except that Compound 4a, 4c, 4d, or 4e was used as the starting material in place of Compound 4b.

[0303]

Examples 17 through 21 Synthesis of (R)-1,1'-bi-(4,6-bis(trialkylsilyl)-2-methoxycarbonyl)naphthyls (6a through 6e)

[0304]



[0305]

In an argon atmosphere, *i*Pr₂NEt (0.51 mL), MeOH (1.0 mL) and DMSO (2.0 mL) were added to a mixture containing one of Compounds 5a through 5e (0.70 mmol), Pd(OAc)₂ (15 mol%), and dppp (16.5 mol%). While the reaction vessel was pressurized to 15 atm under CO atmosphere, the mixture was stirred at 100°C for 24 hours. Subsequently, the reaction mixture was poured into water and the solution was extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the

resulting residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of diethylether/hexane to give Compounds 6a through 6e in yields of 58 to 80%.

5 [0306]

Chemical data for the products of Examples 17 through 21 are shown below.

[0307]

<Product of Example 17 (Compound 6a)>

10 (R)-1,1'-bi-{4,6-bis(trimethylsilyl)-2-methoxycarbonyl}naphthyl: $^1\text{H-NMR}$ (400MHz, CDCl_3) σ 8.34 (2H, s, Ar-H), 8.33 (2H, s, Ar-H), 7.31 (2H, d, $J = 8.4$ Hz, Ar-H), 7.03 (2H, d, $J = 8.4$ Hz, Ar-H), 3.53 (6H, s, CO_2CH_3), 0.57 (18H, s, SiCH_3), 0.30 (18H, s, SiCH_3).

15 [0308]

<Product of Example 18 (Compound 6b)>

(R)-1,1'-bi-{4,6-bis(triethylsilyl)-2-methoxycarbonyl}naphthyl: $^1\text{H-NMR}$ (400 MHz, CDCl_3) σ 8.31 (2H, s, Ar-H), 8.28 (2H, s, Ar-H), 7.32 (2H, dd, $J = 1.2$ Hz, 8.4 Hz, Ar-H), 7.11 (2H, d, $J = 8.4$ Hz, Ar-H), 3.32 (6H, s, CO_2CH_3), 1.12-0.82 (60H, m, SiCH_2CH_3).

[0309]

<Product of Example 19 (Compound 6c)>

25 (R)-1,1'-bi-{4,6-bis(tributylsilyl)-2-methoxycarbonyl}naphthyl: $^1\text{H-NMR}$ (400 MHz, CDCl_3) σ 8.32 (2H, s,

Ar-H), 8.27 (2H, s, Ar-H), 7.32 (2H, d, J = 8.4 Hz, Ar-H),
7.13 (2H, d, J = 8.4 Hz, Ar-H), 3.27 (6H, s, CO₂CH₃), 1.38-0.81
(108H, m, SiCH₂CH₂CH₂CH₃).

[0310]

5 <Product of Example 20 (Compound 6d)>

(R)-1,1'-bi-{4,6-bis(dimethylphenylsilyl)-2-methoxycarbonyl}naphthyl: ¹H-NMR (400 MHz, CDCl₃) σ 8.40 (2H, s, Ar-H), 8.11 (2H, s, Ar-H), 7.52 (2H, d, J = 8.4 Hz, Ar-H),
7.38-7.22 (20H, m, Ar-H), 7.10 (2H, d, J = 8.4 Hz, Ar-H), 3.49
10 (6H, s, CO₂CH₃), 0.70 (12H, s, SiCH₃), 0.37 (12H, s, SiCH₃).

[0311]

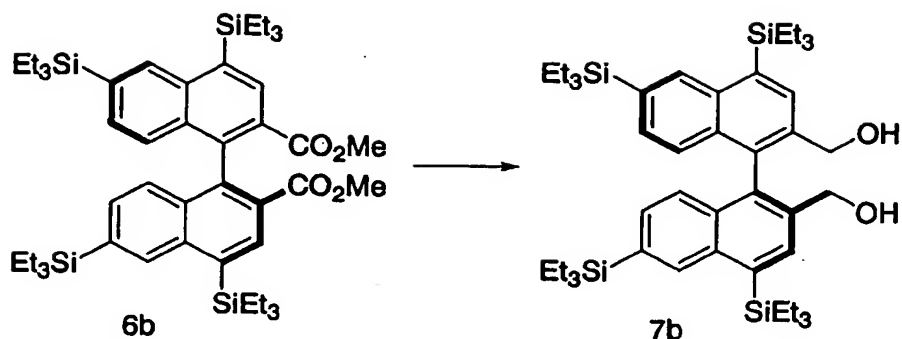
<Product of Example 21 (Compound 6e)>

(R)-1,1'-bi-{4,6-bis(dimethyloctylsilyl)-2-methoxycarbonyl}naphthyl: ¹H-NMR (400MHz, CDCl₃) σ 8.33 (2H, s, Ar-H), 8.30 (2H, s, Ar-H), 7.29 (2H, dd, J = 1.2 Hz, 8.4 Hz, Ar-H), 7.04 (2H, d, J = 8.4 Hz, Ar-H), 3.47 (6H, s, CO₂CH₃),
15 1.43-0.75 (68H, m, SiC₈H₁₇), 0.55 (12H, s, SiCH₃), 0.28 (12H, s, SiCH₃).

[0312]

20 Example 22 Synthesis of (R)-1,1'-bi-{4,6-bis(triethylsilyl)-2-hydroxymethyl}naphthyl (7b)

[0313]



[0314]

In an argon atmosphere, Compound 6b (0.44 mmol) was added to a tetrahydrofuran solution of LiAlH_4 (1.30 mmol) at 0°C , and the mixture was stirred for 1 hour. Subsequently, the reaction mixture was deactivated by sequentially adding MeOH and a saturated aqueous solution of ammonium chloride and the solution was extracted with diethylether. The extract was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. The resulting residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of diethylether/hexane to give Compound 7b in a quantitative yield.

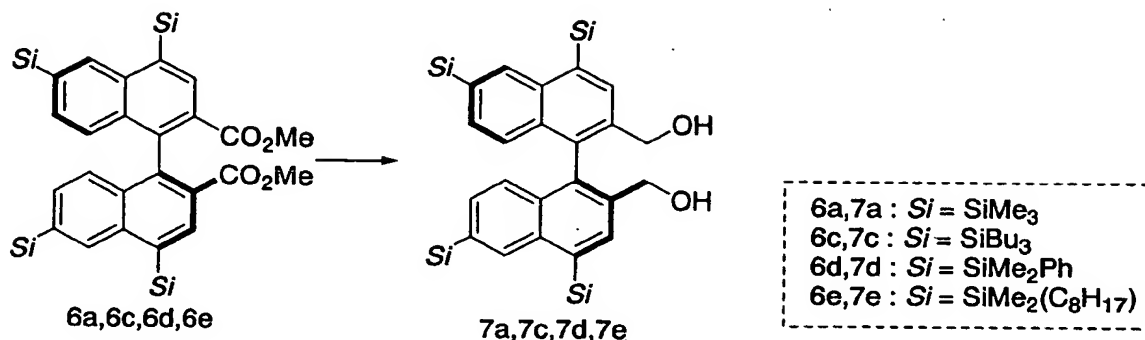
[0315]

$^1\text{H-NMR}$ (400 MHz, CDCl_3) σ 8.31 (2H, s, Ar-H), 7.84 (2H, s, Ar-H), 7.32 (2H, dd, $J = 1.2$ Hz, 8.4 Hz, Ar-H), 7.05 (2H, d, $J = 8.4$ Hz, Ar-H), 4.42 (2H, d, $J = 11.6$ Hz, ArCH_2), 4.16 (2H, d, $J = 11.6$ Hz, ArCH_2), 2.86 (2H, br s, OH), 1.13-0.80 (60H, m, SiCH_2CH_3).

[0316]

Examples 23 through 26 Synthesis of (R)-1,1'-bi-(4,6-bis(trialkylsilyl)-2-hydroxymethyl)naphthyls (7a, 7c, 7d, and 7e)

[0317]



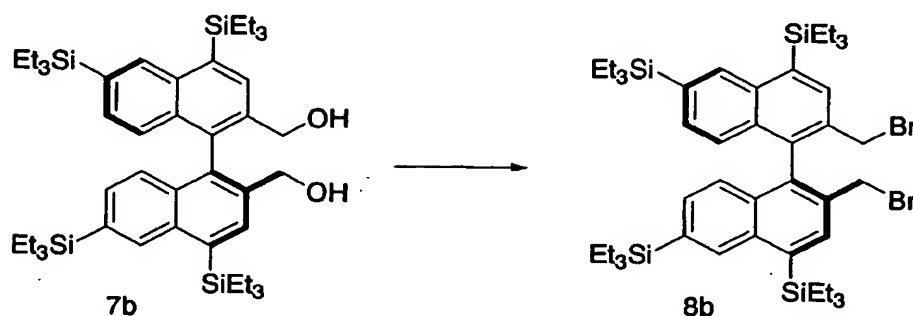
[0318]

To obtain Compounds 7a, 7c, 7d, and 7e in quantitative yields, the same procedure was followed as in Example 22, except that Compound 6a, 6c, 6d, or 6e was used as the starting material in place of Compound 6b.

[0319]

Example 27 Synthesis of (R)-1,1'-bi-(4,6-bis(triethylsilyl)-2-bromomethyl)naphthyl (8b)

[0320]



[0321]

Triphenylphosphine (0.315 g, 1.2 mmol) and carbon tetrabromide (0.398 g, 1.2 mmol) were added to a tetrahydrofuran solution (10 mL) of Compound 7b (0.20 mmol), and the mixture was stirred at room temperature for 4 hours.

5 After completion of the reaction, the reaction mixture was poured into water and was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the residue was subjected to a silica gel
10 column chromatography and was eluted with a hexane solvent to give Compound 8b in a quantitative yield.

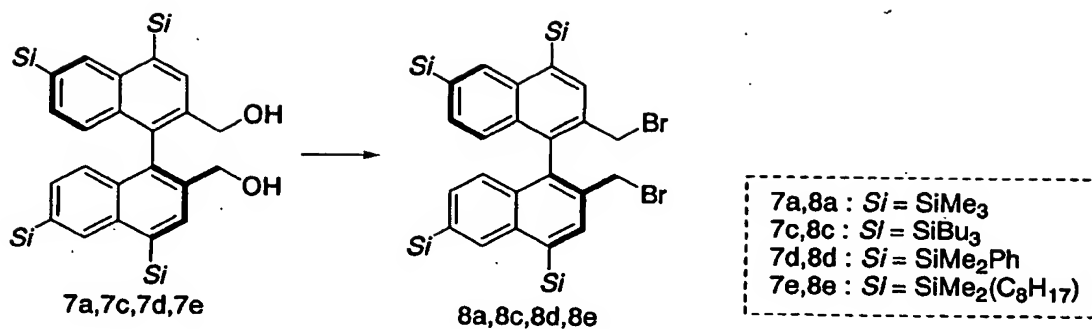
[0322]

¹H-NMR (400 MHz, CDCl₃) σ 8.28 (2H, s, Ar-H), 7.87 (2H, s, Ar-H), 7.34 (2H, dd, J = 1.2 Hz, 8.4 Hz, Ar-H), 7.06 (2H, d, J =
15 8.4 Hz, Ar-H), 4.24 (4H, s, ArCH₂), 1.13-0.80 (60H, m, SiCH₂CH₃).

[0323]

Examples 28 through 31 Synthesis of (R)-1,1'-bi-{4,6-bis(trialkylsilyl)-2-bromomethyl}naphthyls (8a, 8c, 8d, and
20 8e)

[0324]



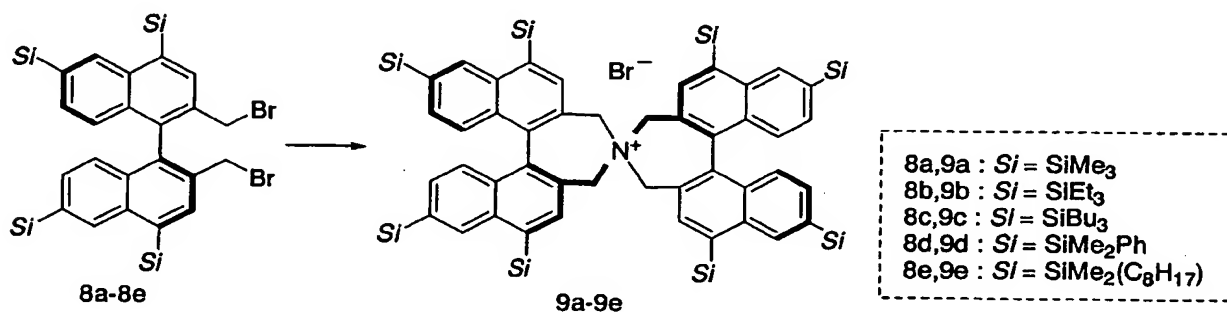
[0325]

To obtain Compounds 8a, 8c, 8d, and 8e in quantitative yields, the same procedure was followed as in Example 27, except that Compound 7a, 7c, 7d, or 7e was used as the starting material in place of Compound 7b.

[0326]

Examples 32 through 36 Synthesis of spiro-bis[[(R)-1,1'-bi-{4,6-bis(trimethylsilyl)naphthyl}}2,2'-dimethyl]ammonium bromides (9a through 9e)

[0327]



[0328]

A 28% aqueous ammonia (0.77 mL, 12.6 mmol) and acetonitrile (5 mL) were added to one of Compounds 8a through 8e (3.15 mmol). The reaction vessel was sealed and the mixture

was stirred for 24 hours while being refluxed. Subsequently, the reaction mixture was poured into water and the solution was extracted with dichloromethane. The extract was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the resulting residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of dichloromethane/methanol to give Compounds 9a through 9e in yields of 25 to 65%.

[0329]

Chemical data for the products of Examples 32 through 36 are shown below.

[0330]

<Product of Example 32 (Compound 9a)>

Spiro-bis[[(R)-1,1'-bi-{4,6-bis(trimethylsilyl)naphthyl}]-

2,2'-dimethyl]ammonium bromide: $^1\text{H-NMR}$ (400MHz, CDCl_3) σ 8.50 (4H, s, Ar-H), 7.80 (4H, s, Ar-H), 7.44 (4H, d, $J = 8.8$ Hz, Ar-H), 7.30 (4H, d, $J = 8.8$ Hz, Ar-H), 4.46 (4H, d, $J = 14.0$ Hz, ArCH_2), 4.10 (4H, d, $J = 14.0$ Hz, ArCH_2), 0.73 (36H, s, SiCH_3), 0.36 (36H, s, SiCH_3).

[0331]

<Product of Example 33 (Compound 9b)>

Spiro-bis[[(R)-1,1'-bi-{4,6-bis(triethylsilyl)naphthyl}]-2,2'-

dimethyl]ammonium bromide: $^1\text{H-NMR}$ (400 MHz, CDCl_3) σ 8.48 (4H, s, Ar-H), 7.91 (4H, s, Ar-H), 7.43 (4H, dd, $J = 1.2$ Hz, 8.4 Hz, Ar-H), 7.25 (4H, d, $J = 8.4$ Hz, Ar-H), 4.38 (4H, d, $J = 13.2$

Hz, ArCH₂), 4.08 (4H, d, J = 13.2 Hz, ArCH₂), 1.32-0.85 (120H, m, SiCH₂CH₃).

[0332]

<Product of Example 34 (Compound 9c)>

5 Spiro-bis[[(R)-1,1'-bi-{4,6-bis(tributylsilyl)naphthyl}}-2,2'-dimethyl]ammonium bromide: ¹H-NMR (400 MHz, CDCl₃) σ 8.47 (4H, s, Ar-H), 7.85 (4H, s, Ar-H), 7.36 (4H, d, J = 8.4 Hz, Ar-H), 7.13 (4H, d, J = 8.4 Hz, Ar-H), 4.39 (4H, d, J = 13.6 Hz, ArCH₂), 4.15 (4H, d, J = 13.6 Hz, ArCH₂), 1.43-0.85 (108H, m, SiCH₂CH₂CH₂CH₃).

[0333]

<Product of Example 35 (Compound 9d)>

Spiro-bis[[(R)-1,1'-bi-{4,6-bis(dimethylphenylsilyl)naphthyl}}-2,2'-dimethyl]ammonium
15 bromide: ¹H-NMR (400 MHz, CDCl₃) σ 8.23 (4H, s, Ar-H), 8.18 (4H, s, Ar-H), 7.57-7.21 (48H, m, Ar-H), 4.61 (4H, d, J = 13.6 Hz, ArCH₂), 4.27 (4H, d, J = 13.6 Hz, ArCH₂), 0.81 (12H, s, SiCH₃), 0.74 (12H, s, SiCH₃), 0.39 (12H, s, SiCH₃), 0.38 (12H, s, SiCH₃).

20 [0334]

<Product of Example 36 (Compound 9e)>

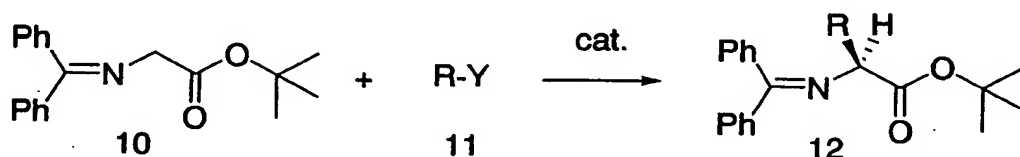
Spiro-bis[[(R)-1,1'-bi-{4,6-bis(dimethyloctylsilyl)naphthyl}}-2,2'-dimethyl]ammonium bromide: ¹H-NMR (400 MHz, CDCl₃) σ 8.47 (4H, s, Ar-H), 7.96 (4H, s, Ar-H), 7.41 (4H, d, J = 8.4 Hz, Ar-H), 7.26 (4H, d, J = 8.4 Hz, Ar-H), 4.43 (4H, d, J = 13.2

Hz, ArCH₂), 4.11 (4H, d, J = 13.2 Hz, ArCH₂), 1.53-0.80 (136H, m, SiC₈H₁₇), 0.73 (12H, s, SiCH₃), 0.70 (12H, s, SiCH₃), 0.35 (12H, s, SiCH₃), 0.34 (12H, s, SiCH₃).

[0335]

- 5 Examples 37 through 52 Asymmetric alkylation using Compounds (9a) through (9e) as an optically active phase-transfer catalyst

[0336]



10 [0337]

At 0°C, Compound 11 (0.6 mmol) of the formula (13) shown as R-Y in Table 1 was added to a mixture of Compound 10 of the formula (12) (0.5 mmol), a phase-transfer catalyst (one of Compound (9a), Compound (9b), Compound (9c), Compound (9d), and Compound (9e)) (0.05 mmol), toluene (3.3 mL), and a 50% aqueous solution of potassium hydroxide (1.0 mL). The mixture was stirred at the same temperature and was poured into water. The solution was extracted with ether and the extract was washed with saturated brine, followed by drying over sodium sulfate and concentration under reduced pressure. The resulting residue was subjected to a silica gel column chromatography to give an alkylated compound 12 of the formula (14). The results obtained for different phase-transfer

catalysts and different alkylating agents were collectively shown in Table 1.

[0338]

The optical purity of the reaction products was
 5 determined according to the technique described in *J. Am. Chem. Soc.* 1999, Vol. 121, No. 27, 6519-6520.

[0339]

Table 1

Examples	R - Y	Cat.	Time [h]	Yield [%]	Ee [%]
37	PhCH ₂ Br	9e	172	96	99
38	"	9d	26	98	98
39	"	9c	50	92	99
40	"	9b	6	97	97
41	"	9a	96	60	92
42	MeI	9e	14	92	93
43	"	9d	16	92	92
44	"	9c	10	93	88
45	"	9b	22	90	89
46	"	9a	10	92	92
47	CH ₂ =CHCH ₂ Br	9e	96	98	98
48	HC≡CCH ₂ Br	9e	32	96	99
49	EtI	9e	10	87	98
50	HexI	9e	10	81	97
51	iPr-I	9e	15	70	95
52	cPent-I	9e	15	75	96

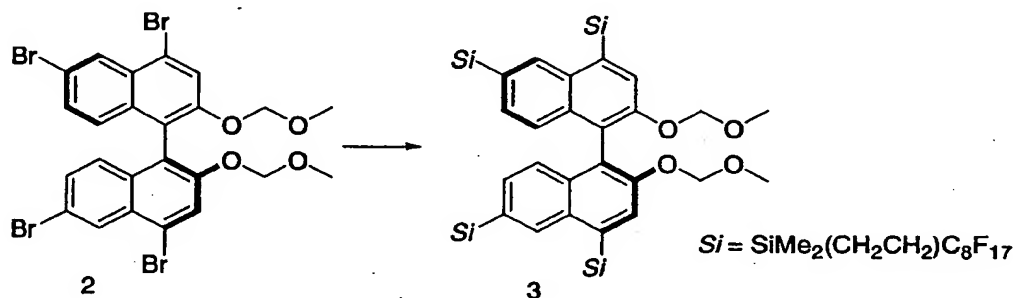
[0340]

The present invention will now be described in further detail with reference to examples of fluorine-containing, optically active quaternary ammonium salts represented by the formula (1b). These examples, however, are provided by way of example only and are not intended to limit the scope of the invention in any way.

[0341]

Example 53 Synthesis of (R)-1,1'-bi-{4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-methoxymethoxy}naphthyl (3)

[0342]



[0343]

In an argon atmosphere, a 1.40M *tert*-butyllithium solution (1.93 mL, 2.7 mmol) was added dropwise to a tetrahydrofuran solution (10 mL) of Compound 2 (0.207 g, 0.30 mol) at $-78^{\circ}C$ and the mixture was stirred for 15 minutes. Subsequently, dimethyl(perfluorooctyl)ethylchlorosilane (1.80 mmol) was added at $-78^{\circ}C$, and the reaction mixture was allowed to warm to room temperature and was then stirred for 4 hours.

p-toluenesulfonic acid monohydrate (0.114 g, 0.60 mmol) was added to Compound 3 (0.30 mmol) in dichloromethane (10 mL) and methanol (10 mL) at room temperature, and the mixture was stirred at 50°C for 24 hours. After completion of the reaction, the reaction mixture was poured into water and was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure to give Compound 4 in a quantitative yield. The chemical data for the product are shown below.

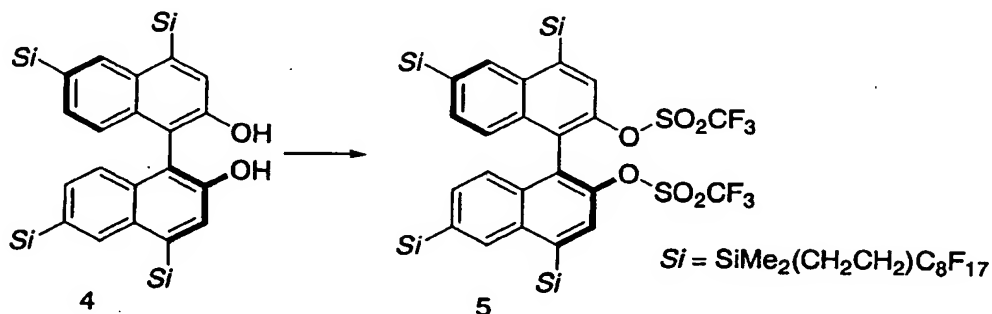
[0348]

¹H-NMR (400 MHz, CDCl₃) σ 8.23 (2H, s, Ar-H), 7.58 (2H, s, Ar-H), 7.39 (2H, d, J = 8.4 Hz, Ar-H), 7.20 (2H, d, J = 8.4 Hz, Ar-H), 5.01 (2H, s, OH), 2.13-1.97 (8H, m, CH₂CF₂), 1.33-1.28 (4H, m, SiCH₂), 1.04-0.99 (4H, m, SiCH₂), 0.61 (12H, s, SiCH₃), 0.37 (12H, s, SiCH₃).

[0349]

Example 55 Synthesis of (R)-1,1'-bi-{4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-trifluoromethanesulfonyl}naphthyl(5)

[0350]



[0351]

In an argon atmosphere, triethylamine (11.1 mmol) was added to a dichloromethane solution (25 mL) of Compound 4 (3.70 mmol), and the mixture was cooled to -78°C.

5 Trifluoromethanesulfonic acid anhydride (11.1 mmol) was added dropwise, and the mixture was allowed to warm to room temperature, followed by stirring for 1 hour. Subsequently, the reaction mixture was poured into a saturated aqueous solution of ammonium chloride and the solution was extracted
10 with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the resulting residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of diethylether/hexane to give Compound 5
15 in a quantitative yield. Chemical data for the product are shown below.

[0352]

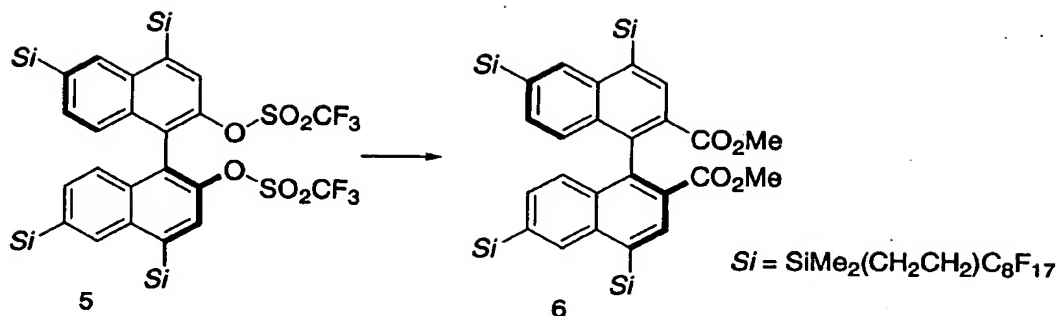
¹H-NMR (400 MHz, CDCl₃) σ 8.33 (2H, s, Ar-H), 7.72 (2H, s, Ar-H), 7.47 (2H, dd, J = 1.2 Hz, 8.4 Hz, Ar-H), 7.32 (2H, d, J =
20 8.4 Hz, Ar-H), 2.05-1.87 (8H, m, CH₂CF₂), 1.35-1.24 (4H, m, SiCH₂), 1.05-1.01 (4H, m, SiCH₂), 0.66 (6H, s, SiCH₃), 0.64 (6H, s, SiCH₃), 0.43 (6H, s, SiCH₃), 0.41 (6H, s, SiCH₃).

[0353]

Example 56 Synthesis of (R)-1,1'-bi-{4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-methoxycarbonyl}naphthyl
25

(6)

[0354]



[0355]

- 5 In an argon atmosphere, iPr_2Net (0.51 mL), MeOH (1.0 mL), and DMSO (2.0 mL) were added to a mixture containing Compound 5 (0.70 mmol), $\text{Pd}(\text{OAc})_2$ (15 mol%), and dppp (16.5 mol%). While the reaction vessel was pressurized to 15atm under CO atmosphere, the mixture was stirred at 100°C for 24 hours.
- 10 Subsequently, the reaction mixture was poured into water and the solution was extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the resulting residue was subjected to a silica gel column chromatography and eluted
- 15 with a mixed solvent of diethylether/hexane to give Compound 6 in a yield of 70%. Chemical data for the product are shown below.

[0356]

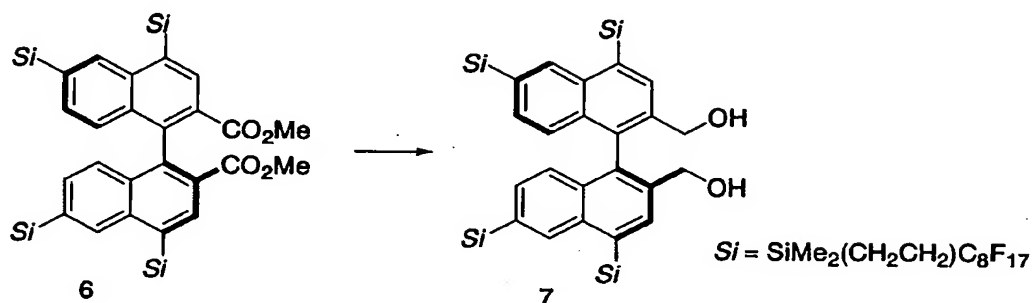
- ^1H -NMR (400 MHz, CDCl_3) δ 8.36 (2H, s, Ar-H), 8.29 (2H, s, Ar-H), 7.33 (2H, d, $J = 8.4$ Hz, Ar-H), 7.23 (2H, d, $J = 8.4$ Hz,
- 20

Ar-H), 3.50 (6H, s, CO₂CH₃), 2.18-1.93 (8H, m, CH₂CF₂), 1.35-1.31 (4H, m, SiCH₂), 1.04-1.00 (4H, m, SiCH₂), 0.53 (12H, s, SiCH₃), 0.38 (12H, s, SiCH₃).

[0357]

- 5 Example 57 Synthesis of (R)-1,1'-bi-{4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-hydroxymethyl)naphthyl (7)

[0358]



10 [0359]

In an argon atmosphere, Compound 6 (0.44 mmol) was added to a tetrahydrofuran solution of LiAlH₄ (1.30 mmol) at 0°C, and the mixture was stirred for 1 hour. Subsequently, the reaction mixture was deactivated by sequentially adding MeOH and a saturated aqueous solution of ammonium chloride and the solution was extracted with diethylether. The extract was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. The resulting residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of diethylether/hexane to give Compound 7 in a quantitative yield. Chemical data for the product are shown

below.

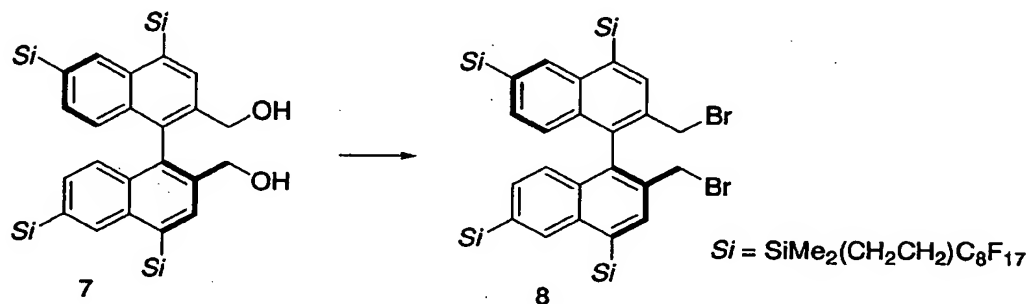
[0360]

¹H-NMR (400 MHz, CDCl₃) δ 8.27 (2H, s, Ar-H), 7.90 (2H, s, Ar-H), 7.33 (2H, d, J = 8.4 Hz, Ar-H), 7.10 (2H, d, J = 8.4 Hz, Ar-H), 4.43 (2H, d, J = 11.6 Hz, ArCH₂), 4.14 (2H, d, J = 11.6 Hz, ArCH₂), 3.20 (2H, br s, OH), 2.16-1.98 (8H, m, CH₂CF₂), 1.34-1.29 (4H, m, SiCH₂), 1.06-1.01 (4H, m, SiCH₂), 0.63 (12H, s, SiCH₃), 0.37 (12H, s, SiCH₃).

[0361]

10 Example 58 Synthesis of (R)-1,1'-bi-(4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-bromomethyl)naphthyl (8)

[0362]



[0363]

15 Triphenylphosphine (0.315 g, 1.2 mmol) and carbon tetrabromide (0.398 g, 1.2 mmol) were added to a tetrahydrofuran solution (10 mL) of Compound 7 (0.20 mmol), and the mixture was stirred at room temperature for 4 hours. After completion of the reaction, the reaction mixture was

20 poured into water and was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium

sulfate and was concentrated under reduced pressure. After concentration, the residue was subjected to a silica gel column chromatography and was eluted with a hexane solvent to give Compound 8 in a quantitative yield. Chemical data for the product are shown below.

[0364]

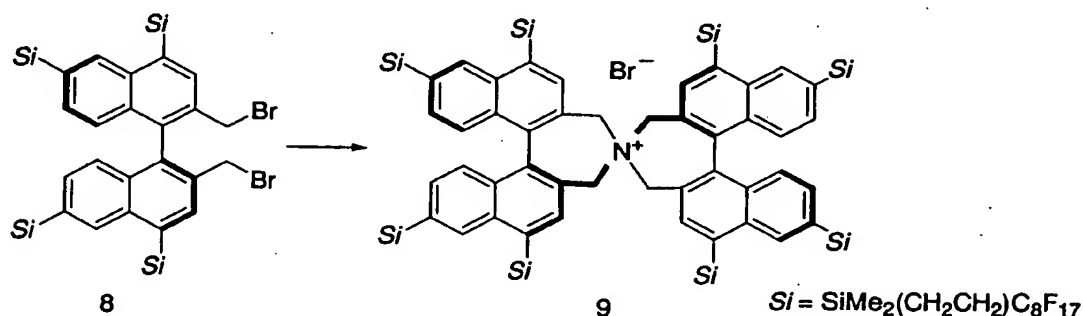
$^1\text{H-NMR}$ (400 MHz, CDCl_3) σ 8.25 (2H, s, Ar-H), 7.89 (2H, s, Ar-H), 7.35 (2H, dd, $J = 1.2$ Hz, 8.4 Hz, Ar-H), 7.09 (2H, d, $J = 8.4$ Hz, Ar-H), 4.23 (4H, s, ArCH_2), 2.17-1.97 (8H, m, CH_2CF_2), 1.34-1.25 (4H, m, SiCH_2), 1.04-1.00 (4H, m, SiCH_2), 0.64 (12H, s, SiCH_3), 0.38 (12H, s, SiCH_3).

[0365]

Example 59 Synthesis of Spiro-bis-{(R)-1,1'-bi-[4,6-bis(2-perfluorooctylethyldimethylsilyl)]naphthyl-2,2'-

dimethyl}ammonium bromide (9)

[0366]



[0367]

A 28% aqueous ammonia (0.77 mL, 12.6 mmol) and acetonitrile (5 mL) were added to Compounds 8 (3.15 mmol). The

reaction vessel was sealed and the mixture was stirred for 24 hours while being refluxed. Subsequently, the reaction mixture was poured into water and the solution was extracted with dichloromethane. The extract was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the resulting residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of dichloromethane/methanol to give Compounds 9. Chemical data for the product are shown below.

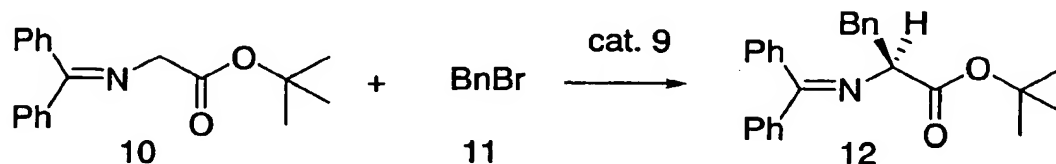
10 [0368]

$^1\text{H-NMR}$ (400 MHz, CDCl_3) σ 8.41 (4H, s, Ar-H), 8.06 (4H, s, Ar-H), 7.39 (4H, d, $J = 8.4$ Hz, Ar-H), 7.25 (4H, d, $J = 8.4$ Hz, Ar-H), 4.48 (4H, d, $J = 13.6$ Hz, ArCH_2), 4.26 (4H, d, $J = 13.6$ Hz, ArCH_2), 2.20-1.98 (16H, m, CH_2CF_2), 1.44-1.40 (8H, m, SiCH_2), 1.07-1.03 (8H, m, SiCH_2), 0.84 (12H, s, SiCH_3), 0.79 (12H, s, SiCH_3), 0.60 (12H, s, SiCH_3), 0.43 (12H, s, SiCH_3).

[0369]

Example 60 Asymmetric alkylation using Compound (9) as optically active phase-transfer catalyst, recovery and recycle of the catalyst

[0370]



[0371]

At 0°C and in an argon atmosphere, benzyl bromide (11) (0.36 mmol) was added to a toluene solution (3.0 mL) of Compound (10) of the formula (12) (0.3 mmol) and Compound (9) of the formula (1) (0.009 mmol). A 50% aqueous solution of potassium hydroxide (1.0 mL) was added dropwise and the mixture was vigorously stirred for 96 hours at the same temperature. Subsequently, the mixture was diluted with water (3.0 mL) and toluene (3.0 mL), and Compound (9) was extracted from the diluted solution with FC-72 (perfluorohexane) (3.0 mL x 3). The fluorous solvent was evaporated under reduced pressure and the remaining residue (quantitatively recovered for use as catalyst) was directly used in the subsequent reaction without further purification. The crude product, which was a mixed solution of toluene/water containing Compound (12) as a primary component, was extracted with ether. The organic phase was washed with saturated brine, dried over sodium sulfate, and concentrated under reduced pressure. The residue was subjected to a silica gel column chromatography to give the alkylated compound 12. The results are shown in Table 2.

[0372]

Example 61

Using the catalyst recovered in Example 60, the same process was repeated in the same reaction scale, followed by the same post-process. The results are also shown in Table 2.

[0373]

Example 62

Using the catalyst recovered again in Example 61, the same process was repeated in the same reaction scale, followed by the same post-process. The results are also shown in Table 2.

[0374]

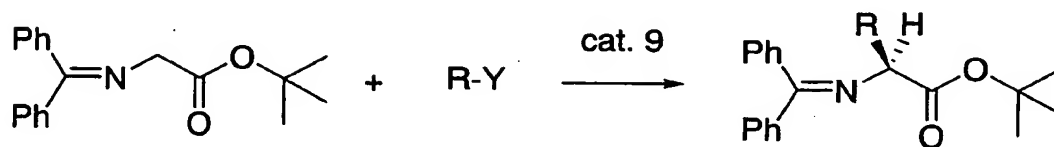
Table 2

	Catalyst 9 (Number of use)	Time (h)	Yield (%)	Optical Purity (%)
Example 60	First time	96	82	90
Example 61	Second time	96	79	92
Example 62	Third time	96	81	92

[0375]

10 Examples 63 and 64 Asymmetric alkylation using Compound (9) as a phase-transfer catalyst

[0376]



[0377]

15 Using Compound (9) as a catalyst, asymmetric alkylation was carried out in the same manner as in Example 60, except that a substrate shown as R-Y in Table 3 was used. The results are together shown in Table 3.

[0378]

Table 3

	R-Y	Time (h)	Yield (%)	Optical Purity (%)
Example 63	$\text{CH}_2=\text{CHCH}_2\text{Br}$	142	80	84
Example 64	$\text{HC}\equiv\text{CCH}_2\text{Br}$	140	81	90

[0379]

The optical purity of the reaction products was determined according to the technique described in *J. Am. Chem.*

5 *Soc.* 1999, Vol. 121, No. 27, 6519-6520.